Analysis of Risk—Update for the Final Rule: Bovine Spongiform Encephalopathy; Minimal Risk Regions and Importation of Commodities

Animal and Plant Health Inspection Service

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I. Introduction

In the November 4, 2003, issue of the *Federal Register*, APHIS published a proposed rule entitled, "Bovine Spongiform Encephalopathy; Minimal Risk Regions and Importation of Commodities" (APHIS 2003c). The rule proposed to amend the regulations regarding the importation of animals and animal products and to recognize a category of regions that presented a minimal risk of introducing bovine spongiform encephalopathy (BSE) into the United States via live ruminants and ruminant products and proposed to add Canada to this category. APHIS also proposed to allow the importation of certain live ruminants and ruminant products and byproducts from such regions under certain conditions.

The rule followed the imposition by APHIS of BSE-related restrictions on Canadian animals and products after the detection of a BSE-infected animal in Canada in 2003 (APHIS 2003a). Prior to the detection of the Canadian case, reported on May 20, 2003, there had been no evidence of BSE in indigenous cattle in North America. Trade restrictions among North American countries were limited to animal disease considerations for diseases other than BSE.

After imposition of restrictions in response to the May 20 report, APHIS conducted a risk analysis to assess the risk of resuming trade in designated commodities and animals in view of the BSE case of Canadian origin in early 2003 (APHIS 2003b, copy provided as Appendix 1). A second case of Canadian origin was reported in the United States on December 23, 2003. After the second case of Canadian origin was reported, APHIS published an explanatory note in February 2004 (APHIS 2004a, copy provided as Appendix 2) in conjunction with a notice of extension of the comment period for the proposed rule (APHIS 2004b). The explanatory note discussed each component of the original risk analysis and related information in light of the new BSE case. Through this evaluation, APHIS concluded that its initial conclusion continued to be appropriate.

APHIS received over 3,000 comments on the November 4, 2003, proposed rule to allow importation of designated ruminants and ruminant products from Canada into the United States (APHIS 2003c). Many of these comments were directed toward the risk analysis (APHIS 2003b) and explanatory note (APHIS 2004a). Consequently, in this update, APHIS is providing additional information on the ability of the existing and proposed mitigations to reduce the risk of BSE introduction and potential for subsequent spread in the United States.

This update extends the analyses APHIS has provided previously. In this update, we summarize the APHIS standards for a Minimal Risk region and the factors considered in our evaluation of such a region and expand on our evaluation of Canada as a Minimal Risk region. In accordance with OIE guidelines (Chapter 1.3.2), the original analysis had four major components: 1) release assessment; 2) exposure assessment; 3) consequence assessment; and 4) risk estimation. We discuss in detail two of these four components – the release assessment and the exposure assessment – and provide, in more depth, data relevant

to our consideration of BSE risk. Finally, we address information that has subsequently become available since the completion of our original analysis.

II. Summary of APHIS' regulatory standards for Minimal Risk regions

In the November 4, 2003, proposed rulemaking (APHIS 2003c), APHIS proposed to define standards for a Minimal Risk region and establish import requirements that imposed additional risk mitigation measures on animals and animal products imported from Minimal Risk regions. The minimal risk standards incorporated the broad elements of the Office International des Epizooties (OIE) guidelines for Minimal Risk regions (OIE 2004a). Below, we provide a discussion of the final standards and a more explicit discussion of how OIE guidelines were incorporated into our considerations in the development of the standards.

In the final rule, the APHIS standards for a BSE Minimal Risk region define it as a region that:

(1) Maintains, and, in the case of regions where BSE was detected, had in place prior to the detection of BSE in an indigenous ruminant, risk mitigation measures adequate to prevent widespread exposure and/or establishment of the disease. Such measures include the following:
   (i) Restrictions on the importation of animals sufficient to minimize the possibility of infected ruminants being imported into the region, and on the importation of animal products and animal feed containing ruminant protein sufficient to minimize the possibility of ruminants in the region being exposed to BSE;
   (ii) Surveillance for BSE at levels that meet or exceed recommendations of the World Organization for Animal Health (Office International des Epizooties) for surveillance for BSE; and
   (iii) A ruminant-to-ruminant feed ban that is in place and effectively enforced.
(2) In regions where BSE was detected, conducted an epidemiological investigation following detection of BSE sufficient to confirm the adequacy of measures to prevent the further introduction or spread of BSE, and continues to take such measures.
(3) In regions where BSE was detected, took additional risk mitigation measures, as necessary, following the BSE outbreak based on risk analysis of the outbreak, and continues to take such measures.

In developing each of these standards for a BSE Minimal Risk region, APHIS based its standards on the guidelines established by the OIE for determining the BSE status of a region. The OIE guidelines, contained in Chapter 2.3.13 of the *Terrestrial Animal Health Code* (OIE 2004a) and supplemented by Appendix 3.8.4 of the Code (OIE 2004b), currently provide for five possible BSE classifications for regions. For each classification, the guidelines recommend different export conditions for live animals and products, based on the risk presented by the region. This framework not only recognizes different levels of risk among regions, but also provides for trade in live animals and products under certain conditions even from regions considered high-risk under the OIE guidelines. In the discussion that

follows, we provide a more detailed discussion of the application of each of these standards with relevance to the OIE guidelines.

(1) Measures in place

A Minimal Risk region must have had in place risk mitigation measures and apply additional measures as appropriate. Such measures are based on risk considerations identified in the OIE *Terrestrial Animal Health Code* Article 2.3.13.2 and embodied in the Article 2.3.13.5, point 1, requirement that a "risk assessment … has been conducted and it has been demonstrated that appropriate measures have been taken for the relevant period of time to manage any risk identified."

OIE measures include (but are not limited to): a broad eradication program and extensive surveillance following the detection of BSE; effective epidemiological investigations with appropriate tracing, control and destruction of risk animals; measures to identify and effectively control pathways for amplification of BSE; continuing risk considerations with corresponding revisions of existing mitigations; processing methodologies; appropriate awareness programs; effective detection and control measures; and veterinary infrastructure sufficient to define and implement these programs. Under APHIS regulations (see (1)(i)-(1)(iii) above), these measures must include: import restrictions, surveillance, and an effective feed ban.

(1)(i) Import Restrictions

APHIS will evaluate the stringency and effectiveness of import restrictions to prevent the importation of BSE infected animals and BSE contaminated products. Our approach reflects the emphasis in the *Terrestrial Animal Health Code* on the evaluation of risk from imports and the need to take appropriate steps to address any identified risk. Specifically, the OIE *Terrestrial Animal Health Code* Article 2.3.13.2 identifies the need to assess the likelihood that a transmissible spongiform encephalopathy (TSE) agent has been introduced via imports and, as mentioned above, Article 2.3.13.5, point 1, emphasizes the need to demonstrate that appropriate measures have been taken.

(1)(ii) Surveillance

An APHIS evaluation of the surveillance program in place within a region will consider whether a region has in place a level of surveillance and monitoring which meets or exceeds the recommendations of OIE *Terrestrial Animal Health Code* Appendix 3.8.4 (OIE 2004b). The OIE recommendations specify approaches to determine whether BSE is present in the country, and, if present, to monitor the extent or evolution of the disease spread. Issues addressed include general principles for examination for clinical signs in relation to statistical approaches to sampling. The recommendations specify the minimum number of cattle exhibiting one or more clinical signs of BSE that should be subjected to diagnostic tests according to the total cattle population over 30 months of age and include recommendations for active targeted surveillance. With respect to the number of samples that must be taken over the preceding 7 years based on the national census of cattle over 30 months of age, APHIS will consider a region to have exceeded the OIE recommendations if the region

samples a larger number of animals than those recommended by OIE over the appropriate period of time. APHIS will also assess policies and practices for active targeted surveillance.

(1)(iii) Feed Ban

APHIS will also consider the effectiveness of a feed ban in place within a region. Determining whether a feed ban has been effectively enforced will involve a review of a number of interrelated factors, including: the existence of a program to gather compliance information and statistics; whether appropriate regulations are in place in the region; the adequacy of enforcement activities (e.g., whether sufficient resources and commitment are dedicated to enforcing compliance); a high level of facility inspections and compliance; accountability of both inspectors and inspected facilities; and adequate recordkeeping. Another indication of an effective feed ban can be derived from epidemiologic investigations of diagnosed cases. Cases of BSE found in animals born after the feed ban was implemented would suggest either that the feed ban was ineffective or that there were noncompliance issues.

Because of the variability in the incubation period of BSE, APHIS chose not to follow the specifications of the OIE *Terrestrial Animal Health Code* (Article 2.3.13.5, point 2) that require a "ban on feeding ruminants with meat-and-bone meal (MBM) and greaves derived from ruminants has been effectively enforced for at least 8 years" [unless the last indigenous case of BSE was reported more than 7 years ago]. Rather, APHIS chose to consider the length of time a feed ban has been in place within the context of the sum total of the control measures in place at the time of the diagnosis of BSE and the actions taken subsequently, recognizing that measures taken with regard to other factors (e.g., inspection practices and level of compliance with the feed ban) may provide more positive evidence than simply the length of the feed ban.

APHIS will consider the factors above as well as region-specific factors—as a combined and integrated evaluation tool—to determine the overall effectiveness of control mechanisms and to analyze the residual risk. In determining whether the measures in place are adequate, APHIS will also consider the BSE incidence within a region with reference to the specific incidence criteria set forth in OIE *Terrestrial Animal Health Code,* Article 2.3.13.5 – i.e., "the BSE incidence rate, calculated on the basis of indigenous cases, has been less than 2 cases per million adult cattle during each of the last 4 consecutive 12-month periods within the cattle population over 24 months of age in the country or zone." In this way, APHIS will examine a combination of factors in a manner that allows us to evaluate an individual country's specific situation, to acknowledge enhanced risk reduction effects of one or more factors that may compensate for other factors, and thereby, to analyze risk based on the overall effectiveness of actions taken by the country to prevent the entry and spread of BSE.

(2) Epidemiological Investigations

APHIS will assess the adequacy and results of any epidemiological investigation conducted by authorities of the region to establish that the standard has been met satisfactorily. Consistent with Article 2.3.13.5, point 2.b. iii of the OIE Code, we will assess whether risk

animals have been identified and controlled and whether the risk animals have been destroyed as appropriate. Appropriate destruction means the animals are prevented from entering the ruminant feed chain—either through controls and restrictions on carcass disposal or through traceback efforts.

(3) Additional Risk Mitigation Measures

During its evaluation, APHIS will determine whether programs such as the ones identified in the OIE guideline are in place and assess their effectiveness. If a region has had a case of BSE within the preceding 7 years or a region has not had a case within the preceding 7 years but has not had an effective feed ban in place for 8 years, the OIE Terrestrial Animal Health Code, Article 2.3.13.5 indicates a region should demonstrate compliance with the measures in points 2 to 5 of Article 2.3.13.2. Points 2 to 5 include an ongoing awareness program for veterinarians, farmers, and workers involved in transportation, marketing, and slaughter of cattle; compulsory notification and investigation of all suspected cases of BSE; a BSE surveillance and monitoring program; and examination in an approved laboratory of brain and other tissues collected within the framework of the surveillance and monitoring system. In addition to consideration of the effectiveness of any of these measures, APHIS will also evaluate factors such as slaughtering and rendering practices, including specified risk materials (SRM) removal; evidence of a broad eradication program; increased surveillance; and additional import restrictions.

III. Release assessment

A release assessment requires consideration of country of origin factors (e.g., incidence/prevalence, surveillance and control programs), biologic factors (e.g., age of animals, agent predilection sites), and commodity factors (e.g., ease of contamination, effect of processing) (OIE Article 1.3.2.4). We considered a number of specific risk factors in the original release assessment, including: incidence of disease in the region of origin; levels of infectious agent; tissue localization; and feed source and exposure. Below, we provide an expanded discussion of these factors as they relate to our evaluation of Canada as a minimal risk region.

III.A. *Considerations Related to Country of Origin Factors*

Country of origin factors encompass a variety of factors such as disease incidence as well as risk mitigation measures. In its previous analyses (APHIS 2003b, 2004a), APHIS observed that the two cases of BSE in Canadian-origin animals, one in May 2003 in Canada and one in the United States in December 2003, satisfied the OIE incidence criterion for a minimal BSE-risk country, currently, less than two cases per million cattle over 24 months of age during each of the preceding 4 consecutive 12-month periods. While we recognize that the number of detected cases does not, by itself, allow for the determination of prevalence, evaluation of existing control measures within a country, including the level of surveillance, provides sufficient information from which to determine the magnitude of the risk. This

section contains more detailed information on several of the factors we considered in making our determination.

III.A.1. Canadian import restrictions

Canada has implemented effective methods for preventing BSE introduction and subsequent potential for spread within Canada in order to minimize the possibility that infected ruminants or contaminated feedstuffs enter the country. The potential for introduction of the BSE agent into Canada has been limited by import restrictions on MBM and live animals. Canada's Animal Disease and Protection Regulations (1978) and Health of Animals Regulations (1991) prohibited importation of MBM from countries other than the United States and, later, from Australia and New Zealand. These rules were first initiated in response to foot-and-mouth disease (FMD) and later extended to address BSE issues.

The Canadian Food Inspection Agency (CFIA) has extensively reviewed its history of imported commodities. CFIA examined transaction records obtained from Canada Customs and Revenue Agency (CCRA) for imports that occurred between 1990 and 2000. Of 4,000 records, 400 potentially represented prohibited material and required further investigation. No records of hazardous imports were discovered and transactions relating to ruminant feed were found to be either misclassifications or incorrectly identified. Further investigation focused on review of Eurostat data (Eurostat 2004) and the import trade data tables provided by Statistics Canada for the period of 1980-2000. References to potential MBM importations from Denmark, France, Belgium, Germany, and Japan, were reviewed in CCRA records and evaluated for MBM and related high risk material. The conclusion of the investigations was that Canada had not imported MBM for use in livestock feed from any country other than the United States, Australia, and New Zealand (CFIA 2002).

In addition, in 2000, Canada conducted a review of products imported from countries of the EU, Scandinavia, and Eastern Europe. The review period covered imports for the years between 1990 and 2000. Original documents with descriptions and volumes held by CFIA veterinary inspectors at ports of entry were investigated. The review concluded that MBM used for livestock feed had only been imported from the United States, Australia, and New Zealand (CFIA 2002).

Canada has not imported live cattle from the United Kingdom (UK) since 1990. In 1994, an import ban was imposed on all countries where BSE had been detected in native cattle, and from 1996 live cattle could only be imported from countries that Canada designated as free from BSE following a comprehensive risk assessment (CFIA 2003a). After detection of BSE in an imported animal in 1993, Canada traced and destroyed and incinerated or repatriated all surviving cattle imported from the UK (Kellar and Lees 2003).

III.A.2. Surveillance in Canada

Canada steadily increased its level of BSE surveillance between 1992 and 2003 (See Figure 1, information provided by CFIA). In calendar year 2003, Canada tested 5,727 cattle. Through

December 1, 2004, a total of more than 15,800 samples had been obtained in 2004 alone, thus exceeding the goal of 8,000. The Canadian surveillance system is ramping up to test 30,000 animals per year in 2005. CFIA officials have stated that this surveillance program is designed to detect one case of BSE in one million adult cattle (CFIA 2004c).

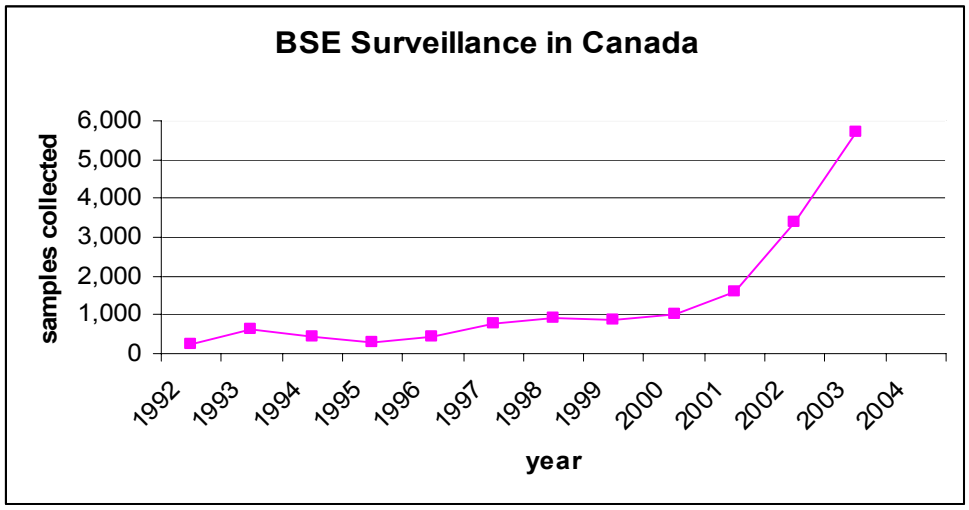

Figure 1. BSE surveillance in Canada for fiscal years 1992-1994 and calendar years 1995-2004.

Canada has an adult cattle population of approximately 5.5 million cattle older than 24 months of age (CFIA 2002). The current OIE Code, Appendix 3.8.4, references adult cattle populations as those greater than 30 months and recommends examining at least 300 samples per year from high risk animals in a country with an adult cattle population of 5 million, or 336 samples per year in a country with an adult cattle population of 7 million. Even though the adult cattle population in Canada is defined as greater than 24 months of age and OIE defines it as greater than 30 months, Canada has met or exceeded this level of surveillance for the past seven years, thus exceeding the OIE guidelines. Active targeted surveillance was begun in 1992, with numbers of annual samples ranging from 225 in 1992 to current levels of several thousand per year. This surveillance has continued to be targeted surveillance, with samples obtained from adult animals exhibiting some type of clinical signs or considered high risk for other reasons that could be considered consistent with BSE.

III.A.3. Feed ban in Canada

The most significant method for preventing the spread of BSE is an effective feed ban. This issue is discussed in some detail in section III.B.3. "Feed source and exposure." Canada has provided information demonstrating that such a feed ban is effectively in place (CFIA 2002, 2003a, 2004b).

Since August 4, 1997, Canada has implemented a ruminant-to-ruminant feed ban that is comparable to that existing in the United States and prohibits the feeding of proteins from ruminant species to ruminant animals (CFIA 2002). This ban prohibits the feeding of ruminant animals with most proteins derived from mammals (excluding proteins derived

from swine and equines only as well as milk, gelatin, and blood products from all species). The CFIA introduced a requirement on October 3, 1997, for the clear identification of all products containing prohibited ruminant materials. Labels and invoices for prohibited material are required to include the statement, "Do not feed to cattle, sheep, deer or other ruminants."

Rendering operations' compliance with the feed ban requirements in Canada is assessed via annual inspections (CFIA 2002, 2004b). A rendering facility must have a permit to operate, and to receive such a permit to operate, rendering operations must meet the manufacturing controls, record-keeping, and labeling requirements prescribed in CFIA regulations. Rendering plants that manufacture both prohibited and non-prohibited material on the same premises must have procedures to keep these materials separated and to prevent cross-contamination. Such procedures include one complete cycle of flushing equipment with a specified quantity of non-prohibited material and handling this material as prohibited material; diverting the initial portion of batches of non-prohibited material to prohibited material storage (the length of time is dependent on the volume contained by the specific piece of the equipment being used and the rate at which the product passes through the equipment); and physical clean-out of the equipment combined with diverting the initial portion of a batch of non-prohibited material to the prohibited material storage.

Based on CFIA inspections, 100 percent of Canadian rendering facilities are in compliance with the ruminant-to-ruminant feed ban requirements applicable to this industry (CFIA 2002, 2004b). As stated in the previous paragraph, rendering facilities must be in compliance to receive or maintain a permit to operate their facility. The ruminant-to-ruminant feed ban that Canada began in 1997 also applied to livestock feed manufacturers and producers who feed livestock. According to CFIA, "feeds for equines, porcines, chickens, turkeys, ducks, geese, ratites or game birds, containing prohibited materials, must be clearly labeled with the following cautionary statement, 'Do not feed to cattle, sheep, deer or other ruminants.'" Labels for bulk feed are stapled to the invoice and shipping documents. Ruminants may be fed pure porcine meal, equine meat meal, and non-mammalian protein meal (fish, avian), as well as milk, blood, gelatin, rendered animal fat and any products produced from these materials from all species" (CFIA 2002). The rules also require that users of livestock feed keep labels or invoices from all purchased feeds containing prohibited material for two years.

Feed manufacturers and retailers are inspected to confirm that feeds are being manufactured, distributed, handled, and used in compliance with the ruminant-to-ruminant feed ban under the CFIA's National Feed Inspection Program (CFIA 2003c). Prior to 2002, Canadian feed mills were comprehensively inspected every three years, although partial inspections could occur more frequently to take samples (e.g. for antibiotic residues), verify labeling compliance, follow up on complaints, or trace back residues. In 2002, however, the CFIA increased the frequency of comprehensive feed mill inspections to one per year.

Compliance issues identified during the course of feed mill and on-farm inspections are required by CFIA to be resolved in a timely manner (CFIA 2002). For example, if unlabeled feeds are found, then the feed is placed under detention and may not be used for any purpose

until the feed is brought into compliance. Inspection and compliance reports are maintained by CFIA.

In summarizing its feed mill inspection program, CFIA reported that "inspections have shown a high level of compliance. Most deficiencies found relate to minor infractions in record-keeping" (CFIA 2002, 2004b). For an annual inspection period of April to March, the fraction of mills reportedly in compliance was 92 percent, 99 percent, and 95 percent for 2002, 2003, and 2004, respectively (CFIA 2004b). CFIA has identified noncompliance of "immediate concern" in fewer than 2 percent of feed mills inspected during 2003-2004 (CFIA 2004b). Those instances of noncompliance of "immediate concern" are dealt with rapidly when identified. Noncompliance of "immediate concern" includes situations where direct contamination of ruminant feed with prohibited materials has occurred, as identified through inspections of production documents or visual observation, and where a lack of appropriate written procedures, records, or product labeling by feed manufacturers may expose ruminants to prohibited animal proteins.

Another indication of an effective feed ban can be derived from epidemiologic investigations of diagnosed cases. Cases of BSE found in animals born after the feed ban would suggest either that the feed ban was ineffective or that there were noncompliance issues. There have been no cases of BSE found in animals born after the feed ban; the only two Canadian BSE cases found were in animals born before the implementation of the Canada's feed ban. Therefore, the Canadian cases of BSE do not provide any evidence of ineffectiveness.

We recognize that, at the time the proposal was published, Canada's feed ban had been in place since 1997, less than the 8 years recommended by the OIE. Based on an analysis of data collected in the UK, the Harvard-Tuskegee Study (Harvard-Tuskegee 2003) estimates that the variability distribution for the BSE incubation period in cattle has a median (50^{th} percentile) of approximately 4 years and a 95^{th} percentile of approximately 7 years. Based on the best-fit parameter values provided in the Harvard-Tuskegee study (Harvard-Tuskegee 2003), the mean (expected value) of the incubation period distribution is estimated at 4.2 years, and 7.5 years (August 1997 through January 2005) represents the estimated 97.5^{th} percentile of the incubation period. Therefore, we determined that the 7-year duration of the feed ban in Canada adequately exceeds the expected BSE incubation period, taking into consideration all of the actions Canada has taken to prevent the introduction and control the spread of BSE (e.g., import controls, level and quality of surveillance, effectiveness of feed ban, epidemiological investigation of detected cases, and depopulation of herds possibly exposed to suspected feed sources).

The discussion above focuses on extrapolation of the data from the UK epidemic to Canada although we recognize that the situations are not identical. The UK epidemic represents the most intense exposure to BSE that the world has seen, and the same level of exposure is not likely to occur in Canada. The expected incubation period could be shorter in the UK, given the higher exposure, than in Canada. However, the combination of all factors considered in Canada, including the fact that Canada implemented a feed ban 6 years prior to identifying the first case, led to our determination that the duration of the feed ban was adequate.

III.A.4. Epidemiological investigations in Canada

Canada conducted rigorous epidemiological investigations after the BSE cases were detected in May 2003 and December 2003 (CFIA 2003b, 2004a). In both instances, the cases were animals that were born before the implementation of the feed ban in 1997, with exposure assumed to occur prior to or near the time of the imposition of the feed regulations. Although a specific source of infection was not identified, the most likely possibility was the introduction of a low level of infectivity into the animal feed supply originating from an infected animal imported from the UK in the period between 1982 and 1989.

The investigations included trace-outs of both cattle that may have been exposed to similar feed sources as the infected animals and of rendered protein products that could possibly have included tissues from the infected animals. The investigation of rendered protein products from the May 2003 case demonstrated that the rendering facility and feed mills involved had good records of compliance with the feed ban, and products were appropriately labeled. Canada carried this investigation down to the on-farm level to evaluate the risk of ruminant exposure to possibly contaminated feed. A survey was conducted of approximately 1,800 sites that were at some risk of having received such rendered material or feed. The survey suggested that 99 percent of the sites surveyed experienced either no exposure of cattle to the feed (96 percent of the sites) or only incidental exposure (3 percent of the sites). The remaining 1 percent represented limited exposure, such as cattle breaking into feed piles, sheep reaching through a fence to access feed, and a goat with possible access to a feed bag. In those instances where the investigation could not rule out the possibility of exposure to the highest risk feed that may have contained rendered protein from the infected animal, the animals in question were destroyed, thus ensuring no further distribution in the food or feed chain (CFIA 2003b). These investigations have resulted in the destruction and sampling of a large number of potentially exposed cattle, and results from all testing have yielded no further evidence of infection. CFIA has traced and destroyed the majority of surviving cattle that were birth cohorts of the two May and December 2003 cases of Canadian origin (CFIA 2003b, 2004a).

III.A.5. Additional risk mitigation measures imposed in Canada

CFIA imposed new regulations to further strengthen its safeguards against BSE. These actions, and others, should serve to reduce any remaining levels of infectivity and the likelihood that infected cattle remain in Canada. Measures taken included requiring the removal of bovine SRM; enhancing enforcement activities associated with the existing cattle ID system; and increasing the level of BSE testing, as described previously. Many of these measures were explained in APHIS' previous risk analyses (APHIS 2003b, 2004a).

In conclusion, all of these factors contribute to the determination that Canada is a Minimal Risk region for BSE. Because Canada implemented import restrictions and a feed ban before the detection of BSE in any indigenous animals, it is more likely that the incidence of BSE in Canada is decreasing (on the down slope of the epidemic curve), rather than increasing (on the up slope). Canada's reported incidence rate of two infected cattle in 2003 out of a

population of 5.5 million adult cattle over 24 months of age (0.4 per million head of adult cattle) is well below the current OIE recommendation regarding incidence in minimal-risk regions. The reported rate of disease cannot be considered independently from either the level and quality of disease surveillance or from the position on the epidemic curve. In this regard, we note that Canada exceeds the OIE recommended level of testing. We also consider Canada's surveillance program for BSE in cattle to be of high quality because it includes active surveillance for BSE in cattle that is appropriately targeted based on known risk factors.

III.B. *Considerations related to biologic factors*

In the original APHIS risk analysis, we discussed the relationship between animal age, infectious dose, and possible levels of infectious agent. The analysis cited research reports demonstrating that the incubation period for BSE is apparently linked to the infectious dose received, i.e. the larger the infectious dose received, the shorter the incubation period (EU SSC 2002). The analysis further indicated that, while some cases have been found in animals less than 30 months of age, these have been relatively few and have occurred primarily in countries with significant levels of circulating infectivity.

The evidence relevant to age and tissue distribution is derived from two types of scenarios. One of these is natural infection, i.e., observing what happened in an outbreak of disease such as that seen in the UK. In this situation, the dose delivered is variable. Cattle may have become infected as a result of receiving low levels of infectious agent for a long period of time, a high infectious dose at a given point in time, or any combination of these two. Data obtained from the outbreak in the UK reflect this scenario and can be used to demonstrate what happens in a real-life situation (see earlier feed ban discussions.) In contrast, the dose administered in the available experimental studies has been a single standard dose given at a single point in time. It may or may not represent a higher dose than those received on the farm. In any event, it is not clear that findings such as incubation period or tissue distribution will be identical in experimental studies and natural infection. For that reason, APHIS attempts to identify whether the information being reported originates from natural infection or experimental challenge.

III.B.1. Age of animal

In natural infections in the UK, BSE was found in animals less than 30 months of age primarily in the late 1980s to early 1990s, during the period in the UK when the incidence of BSE was extremely high in birth cohorts that were exposed when large amounts of the BSE agent was present in feed. From 1988 to 1996, 19 clinical cases of BSE were confirmed in cattle younger than 30 months of age (DEFRA 2003). The youngest confirmed case of BSE was in an animal with clinical disease at 20 months of age in 1992. The last case in an animal aged 30 months or less was in 1996. Data (as of October 1, 2004) on the age of the youngest and oldest cases are presented in Table 1, which is available online at: http://www.defra.gov.uk/animalh/bse/statistics/bse/yng-old.html. Specifically, the table provides statistics derived from both active and passive surveillance activities on the age of

the youngest and second youngest infected animals as well as the oldest and second oldest cases in the UK by year of onset of the disease.

Table 1. Youngest and oldest cases by year of onset

Year of onset	Age youngest case (months)	Age 2nd youngest case (months)	Age 2nd oldest case (years.months)	Age oldest case (years.months)
1986	30	33	5.03	5.07
1987	30	31	9.09	10
1988	24	27	10.02	11.01(2)
1989	21	24(4)	12(2)	15.04
1990	24(2)	26	13.03	14
1991	24	26(3)	14.02	17.05
1992	20	26	15.02	16.02
1993	29	30(3)	14.1	18.1
1994	30(2)	31(2)	14.05	16.07
1995	24	32	14.09	15.05
1996	29	30	15.07	17.02
1997	37(7)	38(3)	14.09	15.01
1998	34	36	14.07	15.05
1999	39(2)	41	13.07	13.1
2000	40	42	17.08	19.09
2001	48	49	15.02	16.09
2002	48	51	16.04	22.07
2003	50	52	18.07	20.06
2004	49	53	16.02(2)	16.03

Note: Numbers listed in parentheses are the number of animals of the same age in cases in which there were more than one.

The age distribution data further show that, of the cattle that developed clinical BSE in the field in the UK epidemic, only 0.01 percent were less than 30 months of age. These observations—from a natural epidemic curve—suggest that the cattle younger than 30 months of age are less likely to be in the later stages of BSE incubation than older BSE-infected cattle, and hence, are less likely to contain high levels of BSE infectivity.

Furthermore, research demonstrates that the incubation period for BSE appears to be linked to the infectious dose of the BSE agent received, i.e., the larger the infectious dose received, the shorter the incubation period. This research also suggests that a calf must receive an oral dose of 100 grams of infected brain material containing high levels of the infectious agent to

produce disease within a minimum of approximately 30 months (EU SSC 2002). Given these observations, scientists who have studied the disease believe that the occurrence of BSE in young cattle is most likely the result of exposure to a very large dose of the BSE agent at a very young age. In other words, identifying cases of BSE in young animals would most likely be the result of either no feed controls or an ineffective feed ban. Therefore, BSE is unlikely to occur in young animals in regions like Canada that have effective feed bans in place.

Not only do the UK data on the age of youngest cases demonstrate an increasing age of cases as the feed bans became effective, suggesting smaller exposures, but also, additional experimental studies in the UK clearly demonstrate a longer incubation period as the exposure dose becomes smaller. This relationship becomes more important when extrapolating the results from the UK BSE pathogenesis studies (Wells, et al. 1994; Wells, et al. 1998; Wells, et al. 1999), all of which were conducted using a relatively large initial oral exposure. All studies of BSE pathogenesis demonstrate the gradual accumulation of BSE infectivity in a non-linear pattern. The amounts of detectable BSE infectivity remain remarkably low for long periods after the initial oral exposure and then increase rapidly as the agent reaches the central nervous system (brain and spinal cord). The pathogenesis studies (discussed in some detail in the following section) demonstrated that clinical signs of neurological disease begin to appear just months after the BSE agent reaches the brain and begins to accumulate. Cattle demonstrating clinical signs of BSE or late in the incubation period clearly represent the greatest risk. Young cattle exposed to low levels of BSE will accumulate very little BSE infectivity within the first few years of life, suggesting that Canadian cattle under 30 months of age are highly unlikely to have accumulated significant amounts of BSE infectivity even if exposed.

III.B.2. Tissue distribution and infectivity

Most of the information on the development and distribution of tissue infectivity in BSE-infected cattle has been derived from experimental pathogenesis studies conducted in the UK (Wells, et al. 1994; Wells, et al. 1998; Wells, et al. 1999). In the studies, cattle were deliberately infected with BSE through oral exposure to the brains of cattle with confirmed BSE. The experimentally infected cattle were killed at regular intervals as the disease progressed. At each interval the tissues of the infected cattle were examined for histopathological changes consistent with BSE and for abnormal prion proteins. Also, at each interval, tissues of the BSE infected cattle were injected into mice to identify those tissues of cattle capable of transmitting the disease.

The pathogenesis studies involved 30 animals, each of which received a large, uniform dose of the BSE agent at a very young age (4 months) (Wells, et al. 1994; Wells, et al. 1998; Wells, et al. 1999). The studies demonstrate that in cattle infected with BSE, the total amount of infectivity in the animal, as well as the distribution of infectivity in the animal's body, change over time (Wells, et al. 1994; Wells, et al. 1998; Wells, et al. 1999). The highest levels of infectivity were detected in the brain and spinal cord at the end stages of disease. Some cattle exhibited clinical signs of BSE as early as 35 months post oral exposure to the BSE agent. By 37 months post oral exposure, all of the five animals that were still

alive demonstrated clinical evidence of BSE. Note that only five animals remained since the other animals had been serially sacrificed at set intervals. Infectivity was found in cattle with clinical signs of BSE in the brain, spinal cord, dorsal root ganglion (DRG)[1], trigeminal ganglia, and the distal ileum of the small intestine.

BSE infectivity was demonstrated in the brain, spinal cord, and DRG as early as 32 months post oral exposure to the BSE agent in some cattle (Wells, et al. 1994; Wells, et al. 1998; Wells, et al. 1999). Infectivity was demonstrated in these tissues three months before animals began to develop clinical signs of the disease. Infectivity was demonstrated in the distal ileum of cattle 6 to 18 months post oral exposure to the BSE agent and again at 38 months and 40 months post oral exposure.

A second phase of the pathogenesis studies, which uses a cattle bioassay as an endpoint, is being conducted to ensure that low levels of infectivity that may not have been detected in the first phase using the mouse bioassay are not missed (UK FSA 2002; EU SSC 2002). The second phase of the study is still underway and is not expected to be completed for several more years. The cattle bioassay, in which tissues from cattle deliberately infected with BSE are injected directly into the brains of BSE-free cattle, is considered to be several hundred-fold more sensitive in detecting BSE infectivity than the mouse bioassay. Preliminary results from the cattle bioassay study demonstrate that, in addition to the materials that were found to contain infectivity when the mouse bioassay was used, the tonsils of calves 10 months post oral exposure to the BSE agent contain infectivity. However, because only one of five animals injected with infected tonsil material developed clinical BSE at 45 months post-inoculation, the level of infectivity in the tonsils appears to be very low. Infectivity studies have also been conducted in cattle exposed to BSE under field conditions. In these animals, at the end stages of the incubation period with demonstrated clinical signs, BSE infectivity has been confirmed only in the brain, spinal cord, and retina of the eye.

As a result of the standardized protocol, the findings may not reflect the development and distribution of infectivity of cattle exposed to BSE under field conditions where the level and age of exposure to the BSE agent are unknown. Furthermore, the pathogenesis studies did not estimate the rate at which the BSE agent increases in tissues with demonstrated infectivity or the tissues that the agent must pass through to reach its ultimate destination in the animal after it is ingested. Despite the information gaps, the results of these studies are useful in that they provide experimental evidence of the distribution of the infective agent in BSE-infected cattle at various stages of the disease and assist in the development of targeted mitigation measures.

BSE infectivity has never been demonstrated in the muscle tissue of cattle examined in either the mouse bioassay or the cattle assays described in the previous paragraphs. Nevertheless, some reports have identified the presence of prions in muscle tissue from rodents, humans, and sheep infected with TSEs other than BSE (Bosque 2002, Prusiner 2004). Although these

[1] DRG are clusters of nerve cells attached to the spinal cord that are contained within the bones of the vertebral column. “DRG” as used in this document has the same meaning as the term “dorsal spinal nerve root ganglia.” Trigeminal ganglia are clusters of nerve cells connected to the brain that lie close to the exterior of the skull.

recent findings suggest the possibility that BSE infectivity might be present in cattle muscle tissue, no such infectivity has been demonstrated in ongoing bioassays. Any theoretical level of infectivity defies quantification, and, if infectivity in muscle tissue occurs, it only represents a miniscule fraction of the total infectivity within affected cattle.

The European Commission's Scientific Steering Committee (SSC) published projections on the proportion of infectivity in certain tissues in 2001 (EU SSC 2001). The SSC, a scientific advisory committee for the European Union, considered the amount and distribution of BSE infectivity in a typical case of BSE and estimated that, in an animal with clinical disease, the brain contains 64.1 percent of the total infectivity in the animal and the spinal cord contains 25.6 percent of the total infectivity. Thus, the brain and spinal cord of cattle with clinical BSE are estimated to contain nearly 90 percent of the total infectivity in the animal.

Furthermore, the SSC estimated that the remaining proportion of infectivity in a typical animal with clinical BSE is found in the DRG (3.8 percent), the trigeminal ganglia (2.6 percent), the distal ileum (3.3 percent), the spleen[2] (0.3 percent), and the eyes (0.04 percent). However, as mentioned above, in experimentally infected cattle BSE infectivity has been demonstrated in the distal ileum as early as 6 to 18 months post oral exposure to the BSE agent and in the tonsils as early as 10 months post exposure. Thus, in younger infected cattle, these materials contain the highest infectivity of the BSE agent. As the infected animal ages, greater levels of infectivity accumulate in the central nervous system tissue as described.

Similar conclusions on the relative infectivity of specific tissues from an infected cow have been reached by Comer and Huntley (Comer and Huntley 2003) in their evaluation of the available literature. Those summary results, presented in Table 2, describe distribution of infectivity in various tissues, i.e., brain, spinal cord, DRG, trigeminal ganglia, tonsil, and distal ileum, of a BSE-infected cow. The table uses an estimated weight of each tissue in grams, the number of estimated ID_{50}/gram, and the total number of ID_{50} attributed to each tissue to estimate a percentage of ID_{50} for each tissue.

Table 2. Infectivity in a clinical case of BSE (bovine oral ID_{50})

Tissue	**Weight**	**Infectivity**		**%**
	g/animal	ID_{50}/g	ID_{50}/animal	
Brain	500	50	25,000	60.2
Spinal cord	200	50	10,000	24.1
Dorsal root ganglia	30	50	1,500	3.6
Trigeminal ganglia	20	50	1,000	2.4
Tonsil	50	0.005	0.25	0.0
Distal ileum	800	5	4,000	9.6
TOTAL	**1,600**		**41,500**	

[2] When this opinion was published, it was based on an assumption that infectivity would be found in spleen—as in other TSEs such as scrapie. However, to date, no infectivity has been found in spleen.

The results of the analysis show that 90 percent of the infectivity is associated with central and peripheral nervous system tissues, i.e., brain, spinal cord, DRG, and trigeminal ganglia. About 10 percent was associated with the distal ileum. Minimal infectivity was associated with tonsils in a clinically affected animal.

III.B.3. Feed source and exposure

APHIS discussed the significance of a feed ban in its previous analyses (APHIS 2003b, 2004a), and we described Canada's feed ban previously in this document. An effective ruminant-to-ruminant feed ban is a crucial element in preventing the establishment of BSE in any country.

Experience in the UK demonstrates that implementation of a ruminant-to-ruminant feed ban exerts downward pressure on the prevalence of BSE (see Figure 2). Animal feed restrictions began in the UK in July 1988, when the use of MBM in ruminant animal feed was banned. In September 1990, the use of Specified Bovine Offals (SBO) was banned for use in any animal feed. This ban prohibited the use in animal feed of bovine tissues with the highest potential concentration of infectivity. As a result of these bans to reduce the recycling of infectivity, the annual incidence of BSE fell by 90 percent between 1992 and 1997 (Harvard-Tuskegee 2003).

When the UK epidemic is plotted by year of birth, the impact of the feed ban is striking. Although the data presented in the following figure and table represent the specific situation in the UK during the years identified in the graph, similar effects (i.e., downward pressure on the prevalence of BSE) could be expected in any country that implements a feed ban.

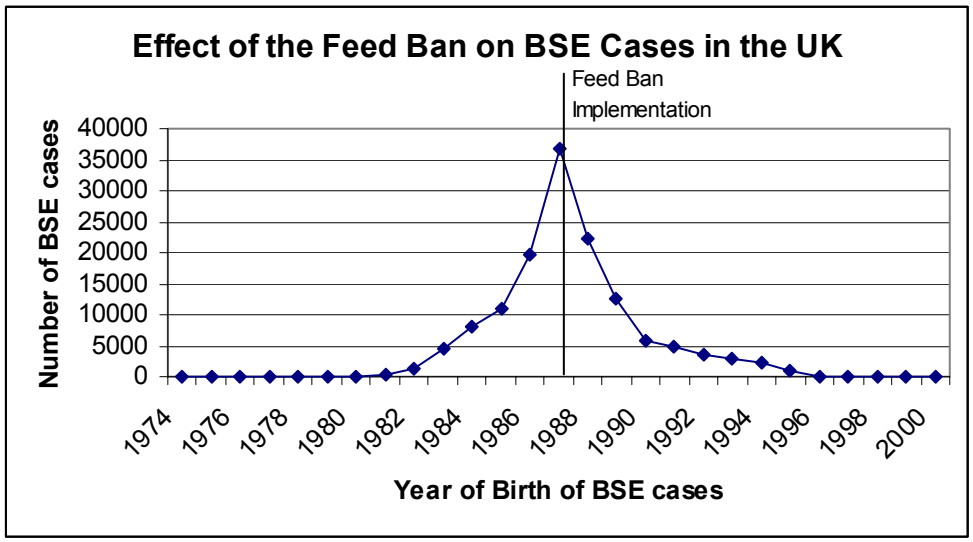

Figure 2. Confirmed cases in UK cattle born after feed ban implementation. **Note:** The first feed ban was implemented in the summer of 1988 (before fall calving). Data available online at: http://www.defra.gov.uk/animalh/bse/statistics/graphs/babs.

The raw data that provided the basis for Figure 2 are reproduced in Table 3 (Available online at: http://www.defra.gov.uk/animalh/bse/statistics/bse/yrbirth.html)

Table 3. Confirmed cases by year of birth, where known

Year	Cases	Year	Cases	Year	Cases
1974	1	1983	4463	1992	3484
1975	0	1984	8069	1993	2945
1976	2	1985	11071	1994	2104
1977	10	1986	19751	1995	1043
1978	6	1987	36927	1996	61
1979	41	1988	22262	1997	36
1980	102	1989	12739	1998	21
1981	262	1990	5738	1999	9
1982	1394	1991	4747	2000	1
Unknown	43336		**Total**: **180625**		

In addition to decreasing the number of cases, an effective feed ban can also influence the length of the incubation period. Research demonstrates that the incubation period for BSE appears to be linked to the infectious dose of the BSE agent received, i.e., the larger the infectious dose received, the shorter the incubation period. This research also suggests that a calf must receive an oral dose of 100 grams of infected brain material containing high levels of the infectious agent to produce disease within a minimum of approximately 30 months (EU SSC 2002). This same evidence is shown through observations from the naturally occurring cases seen in the UK.

Taken together, these statistics demonstrate that, as feed bans were implemented, infection rates dropped. Furthermore, the incubation periods lengthened, which is consistent with experimental findings that the exposure dose is inversely correlated with the length of the incubation period. As feed bans became increasingly effective, the total exposure decreased and the average incubation periods lengthened.

III.C. *Considerations related to commodity factors*

The original release assessment considered both the level of disease occurrence in the country of origin and additional risk mitigation measures that could be applied to further reduce the likelihood of any infectious agent being introduced into the United States via imported animals or animal products. These import restrictions relate to risk factors such as animal age, infectious levels of the BSE agent, and tissue distribution of the BSE agent.

Although APHIS considers Canada to be a Minimal Risk region, the risk of introducing BSE into the United States is further mitigated by imposing import restrictions on animals and animal products from Canada. Compliance with these restrictions must be certified by veterinary officials in Canada.

The risk of introducing BSE infectivity can be reduced by requiring that animals presented for export and animals from which meat or meat products intended for export were derived were subject to a ruminant feed ban. Therefore, the final rule requires that veterinary officials in the country of origin certify that the animals were subject to a ruminant feed ban considered equivalent to that in place in the United States.

Restrictions are imposed on the age of imported animals to further reduce the likelihood of introducing BSE. To ensure compliance with these restrictions, cattle imported from a Minimal Risk region must be accompanied by a health certificate signed by a full-time veterinary official certifying that each animal is less than 30 months of age. In addition, the official veterinarian must certify that the animals have been examined physically and found to be clinically healthy at the time of export. The official veterinarian will reject older, unhealthy animals, thus ensuring that only young, healthy animals will be exported to the United States. As a result of the required inspection and certification, APHIS can have confidence that cattle for export are younger than 30 months of age and have been clinically examined by qualified veterinary personnel. In addition, the Canadian cattle less than 30 months of age were born and raised during a time when the Canadian feed ban had been in place for more than five years, and, based on evidence of a high level of compliance with the feed ban, are unlikely to have been exposed to the BSE agent.

Certification requirements for meat and meat products that are relevant to the animals from which the meat was derived include origin of the animals, limitation to animals subject to an appropriate feed ban, and likelihood of exposure. The risk of introducing BSE infectivity by way of animal products can be further decreased by requiring the removal of SRMs. Therefore, the final rule requires that bovine meat, meat products, and meat by-products must be derived from animals that have had SRMs removed at slaughter.
It is important to note the following change in the final rule. In its proposed rule, APHIS restricted beef imported from Canada to meat derived from cattle under 30 months of age. This requirement has been removed in the final rule, and beef from animals of any age will be allowed to be imported from a Minimal Risk region. As APHIS explained in its notice announcing reopening of the comment period (APHIS 2004b), this change was based on changes that the Food Safety and Inspection Service (FSIS) made in its regulations on January 12, 2004, that now require the exporting country to have an FSIS-equivalent system in place for SRM removal. FSIS did not restrict the age of cattle eligible for slaughter. The role that the age of cattle plays in FSIS actions is in determining whether certain tissues in the animal should be considered SRMs and removed at slaughter. The combined evidence previously discussed demonstrates that meat as an entity is a low risk commodity.

IV. Exposure assessment

In our original exposure assessment, we evaluated the likelihood that infectious levels of BSE would be introduced into the United States from Canada, and the likelihood that BSE would be introduced into commercial animal feed, and, thereby, infect animals. This evaluation was based on multiple factors, each of which reduces risk. These factors include: the potential number of infected animals or products that might conceivably be imported into

the United States from Canada, given the factors discussed in the release assessment; the further reduction in risk associated with imports as a result of the import restrictions imposed by the final rule; the likelihood of tissue from an infected animal entering the U.S. animal feed chain or the human food chain as a result of existing safeguards imposed by USDA and the Food and Drug Administration (FDA); and the likelihood that any such tissue would contain infectious levels of the BSE agent, and be present in sufficient quantities in feed consumed by susceptible animals to cause infection.

Below, we provide an expanded discussion of our exposure assessment. We also include new information provided by Cohen and Gray (Cohen and Gray 2004, copy provided as Appendix 3) in response to comments made on the original risk analysis. We do not repeat information in this section that is discussed earlier in this document related to existing conditions/mitigations in Canada.

IV.A. *Likelihood of tissue from an infected animal entering the food or feed supply*

IV.A.1. Slaughter controls

The Harvard-Tuskegee Study (Harvard-Tuskegee 2003) identified three means whereby infectivity could contaminate edible products. These are emboli in the blood from captive bolt stunning; aerosolization of the spinal cord during carcass splitting; and spinal cord and DRG in meat from the use of advanced meat recovery (AMR). Tissue debris, specifically spinal cord, that accumulates in the carcass splitting saw can be transferred to subsequent carcasses (Helps, et al. 2004).

Recent changes in slaughter plant regulations have reduced the likelihood of contamination from the sources identified in the Harvard-Tuskegee Study (Harvard-Tuskegee 2001, 2003). Studies have found that the use of air-injected pneumatic stunners can cause visible CNS tissue macro-emboli in blood, heart, lung and liver (Anil 1999, Garland 1996). In addition, there is some concern that captive bolt stunners that do not inject air may produce CNS micro-emboli. However, the fraction of brain tissue that the Harvard-Tuskegee Study (Harvard-Tuskegee 2003) estimated would be deposited from these emboli ranged from 0.0133 percent to 0.267 percent. This indicates that air-injected pneumatic stunners present the highest risk of causing CNS tissue emboli in various organs. This risk has been addressed by FSIS regulations (FSIS 2004c) that prohibit the use of air-injected pneumatic stunners in slaughter plants.

Aerosolization of the spinal cord during carcass splitting is a second potential source of contamination identified (Harvard-Tuskegee 2003). The likelihood of this occurring has not been modified by changes in slaughter plant regulations since the time the Harvard-Tuskegee Study (Harvard-Tuskegee 2003) report was written. Nevertheless, Harvard-Tuskegee Study (Harvard-Tuskegee 2003) estimated that the fraction of spinal cord that contaminates muscle during the splitting process is only 0.00108 percent, suggesting that aerosolization is not a significant risk issue.

Cleaning and segregation procedures have reduced the likelihood of contamination from splitting saws (FSIS 2004d, 2004e, 2004f).

At slaughter facilities, FSIS veterinarians can identify and test any suspicious cattle prior to their meat or by-products entering human or animal feed. FSIS has imposed regulations to protect human health that also address animal health issues. As discussed in the explanatory note, the USDA's FSIS amended federal meat inspection regulations to prohibit the use of SRMs for human food and to establish requirements for the disposition of non-ambulatory disabled cattle (FSIS 2004a). FSIS also placed restrictions on the use of advanced meat/bone separation machinery and AMR systems (FSIS 2004b). In July, FDA took similar actions and prohibited the use of certain cattle material in human food, including dietary supplements and cosmetics. Prohibited cattle materials include SRMs, small intestine of all cattle, material from nonambulatory cattle, material from cattle not inspected and passed for human consumption, and mechanically separated beef. These food safety measures have been implemented to protect human health and apply to all meat and meat food products prepared for human consumption in U.S. commerce, including those of Canadian origin.

IV.A.2. Rendering inactivation

The Harvard-Tuskegee Study (Harvard-Tuskegee 2001, 2003) analysis outlined critical elements of the rendering process (Figure 3). That analysis estimated that nearly 95 percent of raw material from ruminants was delivered to rendering plants that processed only prohibited material, while 5 percent of such material was delivered to rendering plants that processed both prohibited and non-prohibited material (so-called mixed plants). Therefore, at the front end of the rendering process, only a very small fraction (0.0001 percent) of prohibited material incorrectly went to rendering plants that processed non-prohibited material.

Within prohibited and mixed rendering plants, a potential hazard is mislabeling of ruminant-derived MBM as non-prohibited. The Harvard-Tuskegee Study (Harvard-Tuskegee 2003) estimated that 95 percent of such MBM is correctly labeled, and 5 percent is mislabeled. In a re-assessment of their estimates, Cohen and Gray (Cohen and Gray 2004, copy provided as Appendix 3) report that the probability of mislabeling at rendering operations is, at worst, 2.3 percent.

Within mixed rendering plants, there is also potential for cross-contamination of non-prohibited material with prohibited material. The Harvard-Tuskegee Study (Harvard-Tuskegee 2003) estimated that such cross-contamination did not occur in 86 percent of lots processed, but could occur among 14 percent of lots processed. In their subsequent re-assessment, however, Cohen and Gray (Cohen and Gray 2004) revised this probability to be, at worst, 1.8 percent.

Although rendering practices vary across rendering plants, the Harvard-Tuskegee Study (Harvard-Tuskegee 2003) estimates that 95 percent of MBM is produced using processes that result in at least a one log reduction in BSE infectivity. Specifically, 5 percent of MBM is rendered using a batch system that reduces infectivity by 3.1 logs; 45 percent of MBM is

rendered using a continuous flow system to which fat is added that reduces infectivity by 2 logs; and 45 percent of MBM is rendered using a continuous flow system without fat added that reduces infectivity by 1 log. Only 5 percent of MBM is rendered using a vacuum system that results in no reduction in BSE infectivity.

The expected (average) reduction in infectivity from rendering is calculated as 1.4 logs. This average effect implies that 97 percent ($10^{-1.4}$) of BSE infectivity is destroyed during rendering and only 3 percent of BSE infectivity survives the rendering process. Taken together with the data suggesting that little infectivity enters the rendering process, only a very small fraction of that survives.

The U.S. feed rule promulgated in 1997 applies to both the rendering and feed manufacturing processes. To ensure compliance with this rule, raw material from ruminants and any protein derived from this is considered prohibited material for ruminant feed. All mammalian protein is considered prohibited material, unless complete separation procedures are maintained sufficient to demonstrate that the mammalian protein is solely porcine or equine protein. Prohibited material must be labeled appropriately throughout the process, from the rendering facility to the finished feed product, to inform users that prohibited feed is only to be fed to non-ruminant species.

The multiple barriers to survival of BSE infectivity through the rendering process suggest that BSE-contaminated materials could "leak" to feed manufacturing only if the BSE agent survives the rendering process and the MBM produced is either mislabeled or cross-contaminated. These pathways for BSE survival are improbable relative to the alternative pathways in which the BSE agent is destroyed, MBM is properly labeled, and no cross-contamination occurs.

IV.A.3. Feed manufacturing controls

Parameter estimates used by the Harvard-Tuskegee Study (Harvard-Tuskegee 2003) represent rendering and feed mixing conditions prior to 2001. The estimate for cross-contamination at rendering is 14 percent (Figure 3) and at feed mixing is 16 percent in facilities that process both prohibited and non-prohibited material (Appendix 1, section 3.16.2 "probContamination" and Appendix 1, section 3.6.3 "probContaminate"). In fact, Cohen and Gray (Cohen and Gray 2004) report that the probability of cross-contamination at rendering and feeding mixing operations is, at worst, 1.8 percent and 1.9 percent, respectively. Downward adjustments to these probabilities support a conclusion that risk of cattle infection is further reduced.

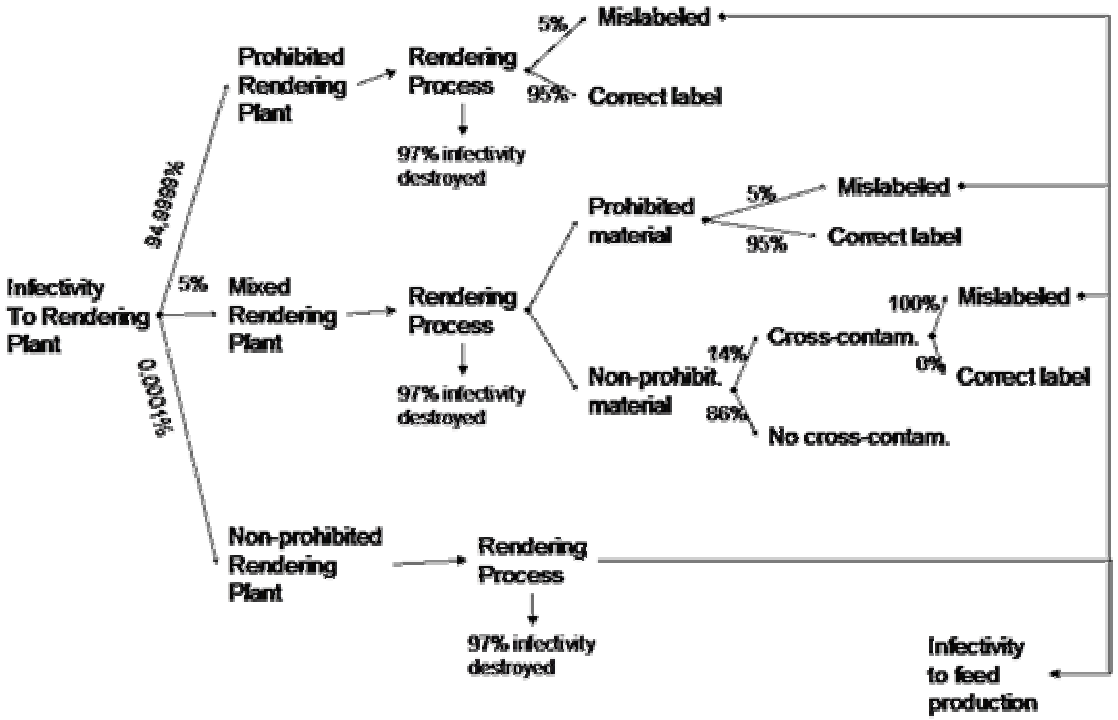

Figure 3. Risk pathway of infectivity during the rendering process (adapted from Harvard-Tuskegee 2003).

In 1997, FDA prohibited the use of all mammalian protein, with the exception of pure pork and pure equine protein from single species processing plants, in the manufacture of animal feeds given to cattle and other ruminants (21 CFR 589.2000, which can be viewed online at http://www.access.gpo.gov/nara/cfr/waisidx_04/21cfr589_04.html). These regulations allow exceptions for certain other products: blood and blood products; gelatin; inspected meat products that have been cooked and offered for human food and further heat processed for feed (such as plate waste and used cellulosic food casings); and milk products (milk and milk protein). Firms must keep specified records on the manufacture of feed, have processes in place to prevent commingling of ruminant and non-ruminant feed containing prohibited materials, and ensure that non-ruminant feed containing materials prohibited in ruminant feed is labeled conspicuously with the statement, "Do not feed to cattle and other ruminants."

Feed manufacturing controls as mandated in FDA regulations further decrease the possibility of spread of the BSE agent. FDA procedures described above are expected to reduce these parameters by requiring segregation of equipment and the processing of prohibited and non-prohibited materials. Nevertheless, some prohibited MBM might cross-contaminate non-prohibited feed or prohibited feed may be mislabeled as non-prohibited.

IV.B. *Likelihood that an animal receives an infectious dose and develops disease*

Several biologic factors influence the likelihood that a bovine animal will receive a sufficient dose of the infectious agent to develop disease. An animal must receive a sufficient dose of BSE infectivity to cause the disease—exposure to levels of the BSE agent below a certain

threshold will not result in infection. The size of the infectious dose depends on the age of the animal. Younger animals appear to be more susceptible, and the animal must live long enough for the BSE infectivity to amplify and manifest the disease.

Experimental challenge studies have been conducted to define the infectious dose (ID) of the BSE agent that must be consumed to cause infection. By definition, a dose of one ID_{50} will infect 50 percent of the animals orally exposed assuming that they are 100 percent susceptible. Susceptibility in cattle declines with age, and therefore animals would be maximally susceptible only at a young age.

Figure 4 illustrates the declining susceptibility of cattle from birth until shortly after 30 months of age. At 30 months, the likelihood of infection stabilizes at approximately 10 percent of the value at one to 12 months of age. Thus, the dose of the BSE agent that would infect 50 percent of adult animals is ten-fold higher than that needed to infect calves (approximately 10 ID_{50}s).

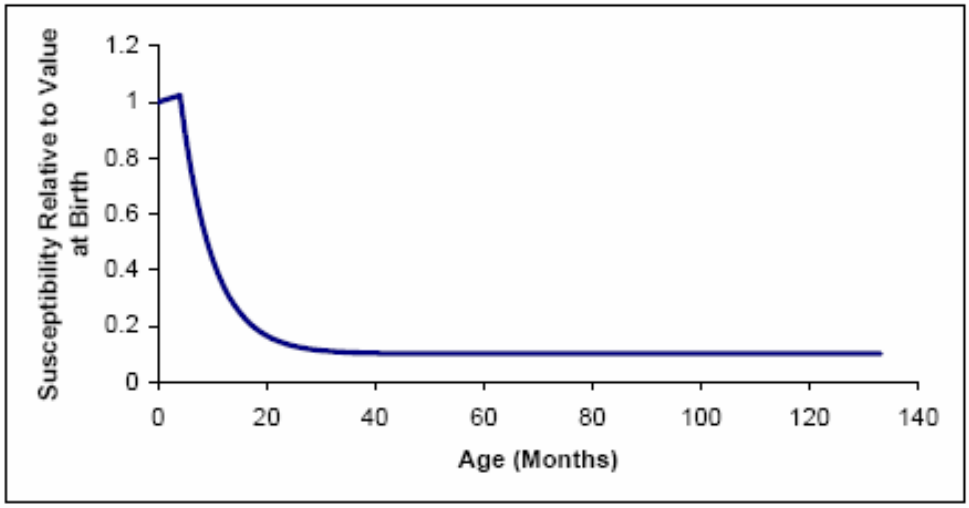

Figure 4. Relative susceptibility to BSE by age curve (from Harvard-Tuskegee 2003).

As discussed below, an infectious dose in contaminated feed must be initially derived from tissues of an infected animal. The upper limit quantity of the BSE agent in an infected animal, estimated through experimental challenge studies, varies with age. In a natural exposure situation, where the average incubation period might be around 60 months, the quantity of the BSE agent in an infected animal is substantially lower in cattle that are under 30 months of age. Figure 5 describes the relationship between time of infection and the fraction of maximal infectivity. This base-case assessment assumes that the maximum amount of infectivity, i.e., infectivity present in all of the tissues of an animal exhibiting clinical signs at the end of the incubation period and therefore at the peak of infectivity, is 10,000 ID_{50}s (Harvard-Tuskegee 2003). At 24 months and 30 months of age—well before the end of the average incubation period—this would translate into a total estimated amount of infectivity of 1.35 and 116.09 ID_{50}s respectively (see Harvard-Tuskegee 2003, section 3.10.2). Therefore, if infected cattle (under 30 months of age) are imported from Canada, the

amount of infectivity that would be available to mix in feed is low even if the entire carcass were rendered and the numerous mitigations described subsequently related to rendering and feed controls were not in effect.

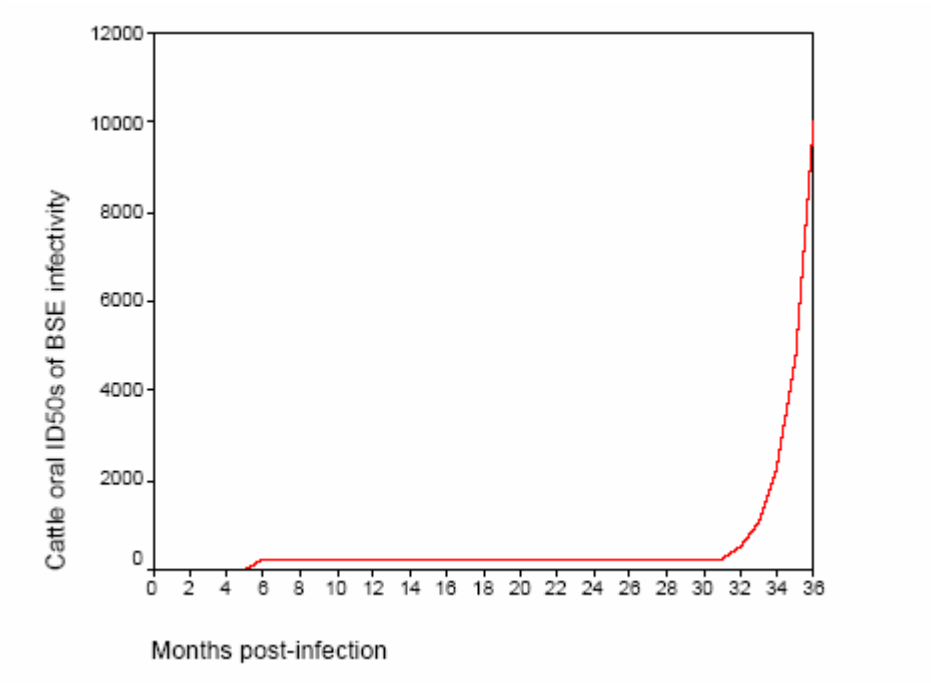

Figure 5. Total infectivity found in calves experimentally infected with BSE, according to months post-infection, expressed in cattle oral infectious dose units where one unit is sufficient to cause infection among 50 percent exposed (ID_{50}s). (Adapted from Morley, et al. 2003 and Harvard-Tuskegee 2001, 2003).

Furthermore, as discussed previously in the section entitled, "Feed ban in Canada," the data from the UK pathogenesis studies (Wells, et al. 1994; Wells, et al. 1998; Wells, et al. 1999) from which the graph presented as Figure 5 is extrapolated must be considered in context. The likely BSE exposure of the two Canadian BSE cases observed to date was much lower than the experimental BSE challenge used in these UK studies given the age of these two cases (greater than 6 years) and the strong likelihood that they were exposed very early in their lives (due to the increased susceptibility of young animals). Low dose exposure to BSE infectivity is likely to result in slower accumulation of total infectivity than the curve illustrated in Figure 5.

Assuming that feeder cattle imported from Canada will be fed and slaughtered in the same way that U.S.-origin feeder cattle are handled, this level of infectivity will be even lower. With this assumption, because most cattle in the United States are generally slaughtered at 16 to 18 months, the infectivity is likely to be nearer one ID_{50} per infected animal carcass. If one ID_{50} will infect 50 percent of the animals exposed when they are 100 percent susceptible, this means all of the available infectivity from one infected animal carcass (and the number of infected animal carcasses is assumed to be minimal) would have to be fed essentially as is

(i.e., no rendering or other processes to reduce infectivity) to one calf to result in infection. This is a very unlikely scenario.

In addition to the low level of infectivity in a carcass based on the age restrictions just described, there would be a dilution or dispersion factor if rendered product derived from this carcass was incorporated into livestock feed. The Harvard-Tuskegee Study (Harvard-Tuskegee 2003) estimates the dispersal of infectivity from one carcass that is rendered and included in a batch of rendered product to be diluted, for example, within a feed mixture to be consumed by 88 head of dairy animals. This estimate is an approximation for infectivity available in feed and indicates that a relatively large number of ID_{50}s would be needed to reach an infective level for one cow.

In summary, the dose received by the animal must be sufficient to cause disease. With decreasing doses and increasing age of the animal at the time of dosing, an animal is less likely to develop disease. The biologic factors as outlined further decrease an already low possibility of a sufficient infectious dose being fed to an animal at a susceptible age to cause disease.

IV.C. *Further post-entry mitigations imposed by the final rule: controls on diversion of imported animals*

The rule requires that live cattle imported from a minimal risk country can only enter the United States for immediate slaughter or for feeding purposes. Movement of these imported cattle is carefully controlled by requiring each animal to have permanent identification that identifies its country of origin, and imported cohorts must only move to slaughter facilities or feedlots with a special permit designed to account for the inventory of cattle consigned to their point of destination. This system of movement control is similar to systems successfully applied for controlling movement and ensuring slaughter of infected cattle in the U.S. tuberculosis and brucellosis eradication programs.

The APHIS rule prevents diversion of imported cattle from slaughter channels. These provisions serve to prevent a BSE-infected animal from by-passing slaughter and living long enough to complete the incubation period and accumulate large amounts of BSE infectivity.

V. Conclusions

V.A. *Cumulative effect of mitigations: series of interlocking, overlapping, and sequential barriers to the introduction and establishment of BSE.*

The total effect of mitigations reflects the combined results of the import restrictions defined in the release assessment and the mitigations described in the exposure assessment. Conceptually, we considered these as a series of five interlocking, overlapping, and sequential risk barriers inserted at critical control points, each of which reduces the risk to the U.S. cattle population. Although we refer to the information considered in the release and exposure assessments in the discussion below, we do not repeat it.

For the purposes of this illustration, we focus on export of live animals from Canada. Similar considerations will apply to commodities. For an infected Canadian animal to transmit infection to a U.S. cow, five barriers must be crossed:

1. U.S. import restrictions
2. Slaughter controls
3. Rendering inactivation
4. Feed manufacturing controls
5. Dose limitations

APHIS recognizes Canada as a minimal BSE risk region and considers it unlikely that BSE infectivity is circulating in Canada because of the control measures that CFIA has implemented. However, even if some infected animals remain, APHIS considers it unlikely that infected animals will be exported because the U.S. import restrictions limit exports to low risk animals.

If, however, an infected animal were to be exported, then each of the remaining barriers outlined above reduces the level of infectivity in the system. Slaughter, rendering, and feed manufacturing controls should remove essentially all of the residual risk in sequence.

Current FSIS slaughter restrictions (FSIS 2004a) in the United States decrease the likelihood that any infectious raw materials from an infected imported animal will be incorporated into the human or animal food supply. Rendering processes in the United States will inactivate significant levels of the agent, further reducing the level of infectivity in MBM. In this regard, the material is treated with heat during rendering in a manner that should destroy much of the remaining infectivity. Furthermore, the bovine material sent to a rendering facility must be kept separate from low risk material and is correctly labeled for use by feed processors.

If a fraction of the hypothetical BSE infectivity were to escape destruction or separation at the rendering facility, it would need to by-pass controls imposed by rendering and feed labeling and usage requirements. Accurate labeling and correct usage at the feed processing facility would further reduce the level of the agent.

If any proportion of infectivity still remained, it would only pose a risk if fed to cattle and an infectious dose was consumed. Feed manufacturing controls in the United States lower the likelihood that contaminated MBM will be incorporated into feed prepared for ruminants. FDA regulations, which apply to all steps in the feed chain, from the rendering facility to the individual producer feeding cattle (21 CFR 589.2000, which can be viewed online at http://www.access.gpo.gov/nara/cfr/waisidx_04/21cfr589_04.html), ensure that ruminant proteins containing infectious levels of the agent will not become incorporated into ruminant feed.

However, if some remaining infectivity were fed to cattle, it would be necessary for a complete infectious dose to be delivered to a susceptible animal. To put it another way, the amount of infectivity present must be adequate to infect an animal ingesting that feed. If the dose is too low, exposure will not result in infection. Animals consuming the infectivity that are older than four months of age are less susceptible than younger animals (16.4 percent at 20 months and about 10 percent in cattle 32 months and older).

Ultimately, however, in the extremely unlikely event that an animal should become infected from contaminated feed, it is unlikely that infectious levels of the agent from that animal would be transmitted to other cattle because infectivity from that animal must also by-pass or circumvent all of the barriers discussed.

Following the final barrier, the residual risk is very small relative to the risk that any infectivity is circulating in Canada. Consider the following hypothetical example: If the elements comprising each barrier allowed as much as 20 percent of the infectivity to pass, the fraction of infectivity potentially introduced into the U.S. cattle herd is 0.03 percent ($[20\%]^5$ or 20 percent to the 5^{th} power) of the original infectivity within the Canadian cattle population. Absent evidence to the contrary, APHIS considers the effect of each barrier to be independent. This simple hypothetical example demonstrates that even moderately effective barriers will substantially reduce risk. Although available data suggest that the true effectiveness of most barriers is substantially greater than 80 percent (i.e., highly effective), the data are not available to estimate with confidence a precise value of effectiveness for each barrier.

V.B. *Summary*

In summary, after evaluation of the information contained in this document, the original risk analysis (APHIS 2003b, copy provided as Appendix 1), the explanatory note (APHIS 2004a, copy provided as Appendix 2), the Harvard-Tuskegee studies (Harvard-Tuskegee 2001, 2003), and the Cohen and Gray memorandum (Cohen and Gray 2004, copy provided as Appendix 3), we conclude that the initial risk estimate for the introduction and establishment of BSE from Canadian sources is appropriate.

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Appendix 1: Risk Analysis: BSE Risk from Importation of Designated Ruminants and Ruminant Products from Canada into the United States

Animal and Plant Health Inspection Service (APHIS)

Veterinary Services

October 2003

Appendix 1: Risk Analysis: BSE Risk from Importation of Designated Ruminants and Ruminant Products from Canada into the United States; Animal and Plant Health Inspection Service, Veterinary Services, October 2003

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Glossary of terms

Air injected stunning: Immobilization process in which a captive bolt gun drives a bolt into the head and fractures the skull, followed by the injection of pressurized air into the cranial cavity, sometimes resulting in emboli that can contaminate various tissues, most importantly and selectively, the liver.

Bovid (bovine): A member of the family bovidae, including cattle, oxen.

Cervid (cervine): A member of the family Cervidae, which includes (but is not limited to) deer, elk, reindeer, moose.

Commercial use: Intended for sale and/or further distribution.

Mechanically separated meat: Process for separating meat from bone using pressurized equipment in which bone fragments can contaminate meat.

Offal: The parts of a butchered animal that are removed in dressing, consisting largely of the viscera and the trimmings, which may include but are not limited to brain, thymus, pancreas, liver, heart, and kidney.

Office International des Epizooties (OIE): The world organization for animal health, located in Paris, France.

Personal use: Items intended only for personal consumption or display and not distributed further or sold.

Rendering: A cooking and drying process that breaks down discarded animal tissues into a protein fraction (e.g., meat-and-bone meal) and a fat fraction (e.g., tallow or lard).

Ruminant: Member of the mammalian suborder Ruminatia; an animal that has a stomach with four complete cavities and that characteristically regurgitates undigested food from the rumen and masticates it when at rest. Such animals include cattle, deer, and oxen.

Segregated facility: A facility that either slaughters only cattle less than 30 months of age or sheep and goats less than 12 months of age or complies with a segregation process approved by the national veterinary authorities of the region of origin and the Administrator as adequate to prevent contamination or commingling of the meat with products not eligible for importation into the United States.

Shooter bulls or shooter bucks: Bulls or bucks harvested by hunters on a game farm or similar facility.

Specified risk materials (as defined in Canada's Health of Animals Regulation): The skull, brain, trigeminal ganglia, eyes, tonsils, spinal cord and dorsal root ganglia of cattle aged 30 months or older; and the distal ileum of cattle of all ages.

Tallow: Solid fat derived through a rendering process from cattle, sheep, etc., used to make candles, soaps, etc.

Traceback: Epidemiological investigation procedure in which efforts are made to identify animals that have been in contact with infected animals or herds in which an infected animal may have resided prior to confirmation of disease.

Traceforward: Epidemiological investigation procedure in which efforts are made to identify animals that have moved out of a herd in which an infected animal resided.

Traceout: Epidemiological investigation procedure in which movement of products and/or animals that might have been exposed to infection is traced.

Trim: Boneless meat cuts (muscle) intended for further processing into a product other than the native form (e.g., hamburger).

Veal calves: Calves that are raised for slaughter at 36 weeks of age or less, the age that represents the industry standard, as a source of veal.

Viscera: Large interior organs in any of the great body cavities, especially those in the abdomen.

Appendix 1: Risk Analysis: BSE Risk from Importation of Designated Ruminants and Ruminant Products from Canada into the United States; Animal and Plant Health Inspection Service, Veterinary Services, October 2003

Executive Summary

The U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS) is conducting a risk analysis as a decision-making tool for a proposal to reinitiate trade in designated ruminants and ruminant products from Canada. Trade in ruminants and ruminant products was banned after bovine spongiform encephalopathy (BSE) was confirmed in a six-year-old cow on May 20, 2003. USDA immediately closed its borders through administrative action and followed that with an interim rule, published May 29, 2003, that added Canada to the list of regions where BSE is known to exist.

Despite the single case of BSE, VS considers Canada as a country that presents a minimal BSE risk for import purposes. The risk assessment provides the rationale for that conclusion, based both on OIE criteria for a minimal risk BSE region and on factors that VS has defined that it will use to address OIE recommendations for a minimal risk region. VS and OIE address the same issues.

The analysis describes the epidemiological characteristics of BSE that are relevant to the risk of imported ruminants and ruminant products from Canada and describes mitigations appropriate to that risk. The commodities discussed in this analysis were relatively freely traded prior to the ban and include feeder cattle and cattle for immediate slaughter less than 30 months of age, cervids and non-cervine ruminants for immediate slaughter, and meat and other products. The mitigations under consideration included a ban on the feeding of material of ruminant origin to ruminants, age restrictions on imported or source animals to an age at which infectious levels of the agent would be unlikely, feed source control, various processing and movement controls, and Canadian Food Inspection Agency (CFIA) verification that the mitigations were applied appropriately.

VS concluded that the surveillance, prevention, and control measures implemented by Canada are sufficient to minimize the risk of importing BSE into the United States, provided that additional mitigation measures are implemented as described. Furthermore, VS concludes that the mitigations that VS proposes are sufficient to allow resumption of trade in these animals and animal products.

Hazard Identification

This is an analysis of the BSE risk that might be posed by importation of designated commodities and animals into the United States from Canada. The only hazardous agent considered in this analysis is BSE. The analysis does not address other transmissible spongiform encephalopathies (TSEs) like chronic wasting disease (CWD) and scrapie that might be endemic in Canada and are also endemic in the United States.

In fact, prior to the confirmation of BSE in Canada and the subsequent implementation of the U.S. ban on ruminants and ruminant products, the United States and Canada traded extensively in animals that were susceptible to BSE, CWD, and scrapie, and products derived from those animals. The U.S. ban on Canadian ruminants and ruminant products was implemented solely because of the change in BSE status in Canada. No such change has occurred in CWD or scrapie status that would warrant their inclusion in this analysis.

BSE is a progressive neurological disorder of cattle that results from infection by an unconventional transmissible agent. Currently, the most accepted theory is that the agent is a modified form of a normal cell surface component known as prion protein, although other types of agents have been implicated, including virinos. The pathogenic form of the protein is both less soluble and more resistant to degradation than the normal form. The BSE agent is extremely resistant to heat and to normal sterilization processes. It does not evoke any detectable immune response or inflammatory reaction in host animals (APHIS 2003c). The disease has been difficult to define experimentally with precision, although risk factors that are independent of the causative agent have been identified and can be mitigated.

Objective

This analysis is being conducted to assess the risk of resuming trade in designated ruminants and ruminant products from Canada to the United States in view of the confirmation of a single case of BSE in Canada in 2003.

On May 29, 2003, USDA published an interim rule adding Canada to the list of countries that are considered to be affected with BSE (APHIS 2003a). On August 26, 2003, based on a thorough scientific analysis, USDA began issuing import permits for certain ruminant derived products from Canada (APHIS 2003b). This analysis is being conducted to determine if, and under what conditions, trade in designated ruminants and ruminant products may be resumed without the need for an import permit. This analysis describes the risk factors associated with those animals and animal products as well as the applicable mitigations.

Because this analysis is conducted to support APHIS rulemaking and because the regulatory authority of APHIS, VS, is limited to animal health issues, the focus of this analysis will be BSE risk to U.S. livestock. The analysis will assess the likelihood that BSE infected animals or animal products would enter the United States from Canada

and expose U.S. livestock by the most likely pathway, that is, through feeding of infected materials to susceptible animals (Prince, et al. 2003; Wilesmith 2001, 2002, 2003).

Because of the limited scope of its regulatory authority, this APHIS analysis will not focus on human health issues, with one exception. Human health issues will be addressed solely in the context of potential exposure of and consequences to humans should BSE-infected material enter the United States AND enter the human food supply. Relevant to this, an evaluation conducted in the context of both human and animal health by the Harvard Center for Risk Analysis (Harvard Center for Risk Analysis et al., 2001) concluded that the United States is highly resistant to spread and establishment of BSE in the unlikely event of its entry into the United States.

Although outside of the regulatory authority of APHIS, the discussion of human health issues is included to maintain compliance with recommendations of the OIE (OIE 2002b), which recommend that animal health import risk analyses address consequences to human health.

Format of the Analysis

This analysis is composed of four components, the release assessment, the exposure assessment, the consequence assessment, and the risk estimation. These components are defined in OIE guidelines and represent the international recommended components for animal health import risk analysis (OIE 2002b).

Release Assessment

The ultimate import risk from imported Canadian animals and products to U.S. livestock is a function of the epidemiological characteristics of the disease and the development and implementation of mitigations to address that risk. This release assessment addresses the following issues:

- Country factors relevant to Canada as a minimal risk country for BSE;
- Epidemiological factors relevant to BSE risk possibly resulting from ruminant trade with Canada;
- Relevant risk mitigations that VS is proposing to apply and the rationale for their use;
- Mitigations that are appropriate to the risk factors identified; and
- Application of these risk mitigation measures on a commodity basis.

<u>BSE detection in Canada</u>

Prior to May 20, 2003, there were no restrictions on trade between the United States and Canada because of BSE. On May 20, CFIA reported a case of BSE in a six-year-old beef cow in northern Alberta (CFIA 2003a). USDA immediately closed its borders through administrative action and followed that action with an interim rule published May 29,

2003 (APHIS 2003a). This rule added Canada to the list of regions where BSE is known to exist and prohibited importation of Canadian ruminants and most products derived from ruminants into the United States.

Canadian response to the incident

Canada conducted an extensive epidemiological investigation after the confirmation of the BSE case on May 20, 2003 (CFIA 2003). The investigation included a consideration of several options for the possible source of exposure to BSE (CFIA 2003), including spontaneous mutation of normal protein to a pathogenic (resistant) form of prion protein or exposure to prions associated with another transmissible spongiform encephalopathy, such as scrapie of sheep and goats or CWD of deer and elk. However, despite exhaustive investigations, CFIA concluded that the scientific evidence to date did not support any of these theories. Furthermore, CFIA noted that the prion associated with the index case was characterized by molecular analysis at the international reference laboratory in the United Kingdom (UK) as BSE, not CWD. Therefore, although it has not been confirmed, the most likely explanation is that the one case resulted from exposure to contaminated feed. The infected animal was born prior to the implementation of a feed ban within Canada and could have been fed contaminated feed at an early age. It is unlikely that a definitive source will ever be firmly established.

Canada as a minimal risk country

Despite the single case of BSE, VS considers Canada as a country that presents a BSE risk for import purposes similar to a minimal risk country as defined by the criteria set by OIE. VS bases this opinion on its evaluation of Canada's basic infrastructure and the control measures which Canada has implemented.

The OIE categorizes countries with indigenous cases of BSE as minimal, moderate, or high risk for BSE, based on established criteria (OIE 2002a). The primary differentiating standard for these designations is the incidence rate of indigenous cases. For a minimal risk country, the incidence rate must have been less than one case per million during each of the last four consecutive 12 month periods within the cattle population over 24 months of age. Canada’s adult cattle population is approximately 5.5 million animals, and only one animal was confirmed with BSE in the last 12 month period. Over the entire preceding three consecutive years, the incidence rate was 0 (zero). This incidence rate is within the parameters for a minimal risk country, and well below the parameters for a moderate risk country.

The only other case of BSE diagnosed in Canada was reported in December 1993 in the Province of Alberta (CFIA 2002). This animal was imported from the UK prior to the ban, so it does not count as an indigenous case that would affect classification is a minimal risk region.

Additional factors relevant to the OIE risk classification include an implementation of an effective ruminant-to-ruminant feed ban, awareness and education programs, compulsory notification of suspect BSE cases, surveillance and monitoring program, an appropriately conducted risk assessment (CFIA 2002), a competent diagnostic capacity, and an appropriate slaughter/culling program to address risk animals when a positive case is identified. Canada fully meets or exceeds all of these factors, with the exception of duration of the feed ban.

Canada has maintained prevention and control measures that were instituted in 1990 to minimize possible exposure and/or amplification of the BSE agent (CFIA 2002; Morley, Chen, and Rheault 2003). Canada has maintained stringent import restrictions since 1990, prohibiting the import of meat-and-bone meal from countries other than the United States, Australia, and New Zealand. Import of live ruminants and most ruminant products have also been restricted to minimize Canada's external risk exposure to BSE. Canada has maintained an active targeted surveillance program in cattle at highest risk for BSE since 1992. Since 1997, Canada has maintained a mammalian to ruminant feed ban, with requirements similar to the feed ban in place in the United States (DHHS).

The single OIE criterion that Canada did not meet at the time this analysis was conducted was duration of the feed ban. The current OIE recommendation (OIE 2002a) is that a minimal risk country should have had an effective feed ban in place for eight years. The current feed ban in Canada has been in place for six years. A strict reading would, therefore, classify Canada as a moderate risk country because the current feed ban has been in place for six years.

VS considers the six year length of the feed ban in Canada as sufficient to classify Canada as a minimal risk region for BSE. The OIE recommendation of eight years may be set at a conservative level to account for the wide range that has been reported for the incubation period of BSE. Because of the variability of current estimates associated with the incubation period for BSE, VS chose not to specify an amount of time that a feed ban should be in place for a minimal risk country. Rather, VS considered the sum total of the control mechanisms (e.g., effectiveness of surveillance, import controls, and feed ban) in place at the time of the diagnosis and the actions taken after it (e.g., epidemiological investigations, depopulation), thereby allowing the actions CFIA took in other elements to compensate for a shorter feed ban. As an example relevant to this point and discussed in more detail elsewhere in this document, the level of surveillance conducted in Canada exceeded the OIE recommendations. In addition, Canada's surveillance was both active and targeted in such a manner as to exceed the OIE recommendations. VS considers Canada to exhibit minimal risk for BSE even though the feed ban has not been in place for eight years because Canada has compensated in the areas of surveillance and control.

VS considers OIE recognition of status in developing trade policies. However, VS is aware that OIE recommendations are evolving. In fact, VS has proposed revisions of the OIE recommendations for BSE and has made comments to reflect this through official channels. VS is concerned that some OIE criteria may be too general and others too

specific. At one end of the spectrum, the OIE criterion stating that "a risk assessment…has been conducted and it has been demonstrated that appropriate measures have been taken for the relevant period of time to manage any risk identified" (OIE 2002a) appears to be extremely general. On the other end of the spectrum, as discussed previously, the requirement that "the ban on feeding ruminants with meat and bone meal and greaves derived from ruminants has been effectively enforced for at least 8 years" may be too restrictive when other factors are considered.

VS definition of BSE minimal risk region

Therefore, VS has developed a list of factors that a country or region should address that VS will use to evaluate whether the region exhibits minimal risk for BSE. These factors address the same issues as OIE recommendations and include two categories of regions:

- Regions in which a BSE-infected animal has been diagnosed but in which measures have been taken that make it unlikely that BSE would be introduced from the region into the United States, and
- Regions in which BSE has not been detected but which cannot be considered BSE free. For example, such regions might have exhibited some level of risk resulting from factors like limitations in the surveillance program or import requirements that are less restrictive than those of the United States. However, the region took sufficient measures to be considered minimal risk, such as increasing its level of surveillance or import restrictions to the point that risk of BSE introduction from the region is unlikely. However, the region has not had the mitigations in place long enough to be considered BSE-free.

Specifically, VS proposes that a BSE minimal-risk region is a region that:

(1) Maintains, and, in the case of regions in which BSE was detected, had risk mitigationmeasures in place prior to the detection of BSE in the region that were adequate to prevent widespread exposure and/or establishment of the disease.

This factor is important in identifying regions in which a BSE outbreak is unlikely to occur, or, if an outbreak does occur, in which it is likely to be limited. If a region maintains controls designed to contain BSE introduction or exposure of animals, and, in those regions where BSE has been detected, if the region had such controls in place at the time of detection, it is more likely to present minimal risk than a region that does not have such controls in place. According to the VS definition of BSE minimal risk region, such measures would include import restrictions, surveillance, and a feed ban, as follows:

> (a) The region had restrictions on the importation of animals that were sufficient to minimize the possibility of infected ruminants being imported into the region and restrictions on importation of animal products and animal feed containing ruminant protein that were sufficient to minimize the possibility of ruminants in the region being exposed to BSE.

This factor addresses whether the region faces a high risk of initial or recurrent BSE outbreaks from multiple importations of animals or products that may spread BSE. In those regions in which BSE has been detected, it addresses whether the region's BSE outbreak was more likely to be the result of a point failure in its import controls or possible exposure prior to the implementation of such import controls. Because the incubation period for BSE is generally measured in years (OIE 2002a), the finding of a case of BSE reflects an exposure that occurred several years in the past.

(b) The region conducted surveillance for BSE at levels that meet or exceed OIErecommendations;

This factor addresses the question of whether BSE is or would be likely to be quickly and reliably identified in a region (a situation that would support a minimal risk designation) or whether lack of effective surveillance suggests the possibility that BSE-infected animals may be overlooked so that the scale of the a problem may be greater than officially recognized.

(c) The region has a ban on the feeding of ruminant protein to ruminants that appears to be an effective barrier to the dissemination of the BSE infectious agent in place, and compliance with the ban appears to be good.

This factor distinguishes between regions with effective feed bans and those without them. If an animal with BSE were born after a feed ban was implemented, the observation suggests that the feed ban may not have been effectively enforced.

(2) In regions in which BSE was detected, the epidemiological investigation conducted following detection of BSE was sufficient to confirm the adequacy of measures to prevent the further introduction or spread of BSE, and the region continues to take such measures.

This factor addresses whether a region adequately investigates a case of BSE to determine if any of the risk factors have changed. If there have been any significant changes in risk factors, there might be a possibility of increased incidence of BSE.

(3) In regions in which BSE was detected, additional risk mitigation measures were taken, as necessary, following the BSE outbreak. These were based on risk analysis of the outbreak, and the region continues to take such measures. The additional measures reflect lessons learned during the outbreak and incorporation of policies developed from consideration of new or additional technical information into existing programs.

This factor addresses whether a region implements all necessary risk mitigation measures to prevent further exposure to BSE. It distinguishes between those regions that thoroughly analyze their situation and that address the relevant problems from regions

that do not impose risk mitigation measures, thus prolonging possible exposure to BSE. Each factor of this definition is repeated below, and the observations relevant to Canada as a minimal risk country are discussed.

(1) A region maintains in which BSE was detected had risk mitigation measures in placeadequate to prevent widespread exposure and/or establishment of the disease prior to the detection of BSE in the region, and it continues to maintain these restrictions.

(a) The region had restrictions on the importation of animals that were sufficient to minimize the possibility of infected ruminants being imported into the region and restrictions on importation of animal products and animal feed containing ruminant protein that were sufficient to minimize the possibility of ruminants being introduced into the region or ruminants in the region being exposed to BSE.

Canada has maintained stringent import restrictions since 1990 (CFIA 2002; Morley, Chen and Rheault 2003). These restrictions prohibited the importation of live ruminants and most ruminant products from countries that had not been recognized as free of BSE by the United States, Canada, or Mexico. These countries have had an agreement to recognize country evaluations conducted by any of the others.

Canada prohibited the importation of live cattle from the UK and the Republic of Ireland starting 1990, and subsequently applied the same prohibitions to other countries as those additional countries identified native cases of BSE. In 1996, Canada's policy became even more restrictive and it prohibited the importation of live ruminants from any country that it had not recognized as free of BSE.

Some animals were imported into Canada from high risk countries prior to the imposition of these import restrictions. A total of 182 cattle was imported into Canada from the UK between 1982 and 1990. In actions similar to those taken in the United States, efforts were made in Canada to trace these animals. In late 1993, after Canada identified a case of BSE in one of the imported cattle, all cattle imported from the UK or the Republic of Ireland that remained alive at the time were killed (CFIA 2002).

Import restrictions have also been imposed on ruminant products, including the one that was imposed on meat-and-bone meal in 1978 (CFIA 2002). In general, Canada has prohibited the importation of most meat-and-bone meal from countries other than the United States, Australia, and New Zealand. Limited amounts of specialty products of porcine or poultry origin were allowed to be imported into Canada under permit for use in aquaculture feed products. No meat-and-bone meal for livestock feed-associated uses has been imported, except from the United States, Australia, and New Zealand.

(b) The region conducts surveillance for BSE at levels that meet or exceed OIE recommendations for surveillance for BSE.

OIE recommendations are recognized by the World Trade Organization as international

recommendations for animal disease control. One OIE criterion for a BSE minimal risk region is that surveillance for BSE must have been conducted for at least seven years (CFIA 2002a). Canada has conducted such surveillance since 1992. The OIE Code (OIE 2002c) provides guidelines for surveillance and monitoring systems for BSE, identifying the minimum number of annual investigations recommended based on the adult cattle population of a country. To meet this recommendation, Canada would have to test a minimum of 336 samples annually since the country has a population of 5.5 million adult cattle. Canada has tested more than this minimum number of samples for the past seven years (CFIA 2002). Therefore, Canada exceeds the basic requirements for this criterion. In addition, Canada exceeds other OIE criteria by conducting active targeted surveillance, rather than routine surveillance. In this regard, active targeted surveillance involves sampling animals at risk for BSE, even if there is no evidence of clinical signs.

(c) The region has implemented a ban on the feeding of ruminant protein toruminants that appears to be an effective barrier to the dissemination of the BSE infectious agent. There is no evidence of significant non-compliance with the feed ban.

Canada implemented its feed ban in 1997 (CFIA 2002a). The ban prohibits the feeding of most mammalian protein to ruminants. The conditions of the ban are such that VS considers them to exceed minimal recommendations for a feed ban prohibiting feeding of ruminant material to ruminants. Under the ban in place in Canada, mammalian protein may not be fed to ruminants with certain exceptions. These exceptions include pure porcine or equine protein, blood, milk, and gelatin. The feed ban is essentially the same as the feed ban in place in the United States (DHHS). Relevant to the date of implementation of Canada's feed ban, the animal in which BSE was diagnosed in May 2003 was a six-year-old native-born beef cow from the Province of Alberta that was born before implementation of the feed ban (CFIA 2003a).

Canadian government authorities inspect rendering facilities, feed manufacturers and feed retailers to ensure compliance with the feed ban (CFIA 2003a). Rendering facilities are regulated under an annual permit system, and compliance with the regulations is verified through at least one inspection each year. Feed manufacturers or mills, feed retailers, and farms have been inspected on a routine basis. These inspections have revealed that the level of compliance is good, and there is no evidence of significant noncompliance with the feed ban (CFIA 2003a).

(2) In a region in which BSE has been detected, the epidemiological investigationfollowing detection of BSE was sufficient to confirm the adequacy of measures to prevent the further introduction or spread of BSE, and the region continues to take such measures.

Canada conducted an extensive epidemiological investigation after the single case of BSE that was detected in May 2003 (CIFA 2003a). This investigation included detailed tracebacks to identify possible herds of origin of the infected animal, traceforwards from the infected herd, and traceforwards of any possible feed or rendered material derived

from the carcass of the infected animal. Fifteen premises were quarantined as part of the traceback and traceforward investigations, and cattle on the quarantined premises were slaughtered. Additionally, cattle that were identified as having moved from a quarantined herd to another herd were slaughtered.

The potential for exposure resulting from use of rendered material or feed that could have been derived from the carcass of the infected cow was investigated. Using a broad definition of exposure that would include all possible exposures, the rendered material could have been distributed to approximately 1,800 sites. These included 600 facilities that receive bulk shipments of either rendered protein or feed and 1,200 individual producers or consumers who purchased finished feed by the bag. A survey was conducted of those entities that were at some risk of having received such rendered material or feed. The survey results suggested that 99 percent of the sites surveyed had no exposure to feed (96 percent of the sites) or only incidental exposure (3 percent of the sites). The remaining 1 percent had limited exposures, examples of which included cattle breaking into feed piles, sheep reaching through a fence to access feed, and a goat with possible access to a feed bag.

The investigation included a consideration of several possibilities for the source of exposure to the infected cow (CFIA 2003). Although it has not been confirmed, CFIA assumed, based on the age of the cow, that the animal was exposed through contaminated feed. The infected animal was born prior to implantation of the feed ban in Canada and could have been exposed to contaminated feed at an early age (CFIA 2003a).

The renderers and feed mills that were included in the investigation had records of compliance with the feed ban. The on-farm inquiries revealed a very small probability of exposure of ruminants to prohibited feed. Although the possibility exists that the original source of the BSE agent could have been imported, there was no evidence that this resulted from an illegal import. The BSE agent could have originated from animals imported from the UK prior to implementation of import restrictions in 1990. The surveillance program was sufficient to confirm the continued existence of adequate measures to prevent further introduction or spread of BSE.

(3) In a region in which BSE has been detected, the region took additional risk mitigation measures, as necessary, following the BSE outbreak that were based on risk analysis of the outbreak, and it continues to take such measures.

Following the detection of BSE in Canada, a broad eradication program was initiated during the epidemiological investigation. More than 2,700 head of cattle were culled. As part of the culling activity, more than 2,000 animals that were 24 months of age or older were tested. The 700 that were not tested were less than 24 months of age. No further evidence of BSE was detected in any of these animals.

In addition, Canada prohibited the use of certain tissues, which have been called specified risk materials, in the human food supply (CFIA 2003). These are tissues in which the infectious agent has been shown experimentally to localize.

As noted previously, Canada has maintained an effective mammalian-to-ruminant feed ban, with requirements similar to the feed ban in place in the United States (DHHS), since 1997. Since compliance with the feed ban appears to have been good (CFIA 2003a), it is unlikely that the animal recently confirmed with BSE ingested contaminated feed during the period covered by the ban. This suggests that the ban has been effective. All of these actions will further reduce the already minimal risk of the spread of BSE.

Because we believe that regions such as Canada, that can effectively address the factors listed above, pose a minimal risk of introducing BSE into the United States, we believe it is warranted to allow the importation of designated commodities from such regions. These are prohibited importation from regions in which BSE exists and regions that present an undue risk of BSE under our current regulations (APHIS 2003). However, because BSE was diagnosed in at least one animal in the region, we believe it is necessary to continue to take precautions to further mitigate the chance that BSE might be introduced into the United States from the region. The precautions appropriate for specific commodities intended for importation would be determined by the presence or absence of factors that make it more or less likely the commodity might be contaminated or infected with the BSE.

We are conducting this analysis based on our consideration of Canada as a minimal risk region for BSE. We are addressing individual commodities in this analysis because the BSE commodity import requirements that we intend to propose based on this analysis, while similar to the OIE recommendations (OIE 2002a), are somewhat more stringent than those of OIE.

Risk Factors

As previously mentioned, the nature of the BSE infectious agent has not been confirmed with certainty. However, it has been possible to define risk factors that contribute to establishment and spread of BSE. These factors are based on technical knowledge and disease epidemiology and do not require definition of the nature of the agent. Therefore, the mitigation approaches described in this document should be effective regardless of the nature of the BSE agent.

The following discussion will address risk factors that are relevant to BSE contamination of commodities (both animals and products) that might be exported from Canada to the United States. The overall risk concern is whether the imported commodities are likely to contain infectious levels of the agent, enter the U.S. animal feed supply, and be able to infect animals.

BSE is a difficult disease to define experimentally with precision because of the long incubation period and limitations in experimental models. Controlled studies are often difficult to conduct because of the studies take so long to complete. Much of the data

originate from epidemiological observations made during BSE outbreaks. The time necessary to conduct epidemiological studies in animal may be years.

Therefore, although risk factors can be identified with some certainty, individual risk mitigation measures may be difficult to apply precisely. For example, the discussion in this document will identify contaminated feed as the most likely pathway of BSE transmission. However, it has not been established with certainty that contaminated feed is the only pathway. Furthermore, it cannot be assumed that there is complete compliance with a feed ban, which is the most effective mitigation for contaminated feed. Therefore, VS considered it necessary to mitigate risk arising from alternative pathways or lack of compliance with a feed ban.

Feed source and exposure

The primary source of BSE infection is commercial feed contaminated with the infectious agent. Scientific evidence (Wilesmith, et al. 1988; 1991; 1992) shows that feed contamination results from the incorporation of ingredients that contain ruminant protein derived from infected animals. Standard rendering processes do not completely inactivate the BSE agent. Therefore, rendered protein such as meat-and-bone meal derived from infected animals may contain the infectious agent. Bans prohibiting incorporation of mammalian or ruminant protein into ruminant feed are imposed to mitigate risk.

Oral ingestion of feed contaminated with the abnormal BSE prion protein is the only documented route of field transmission of BSE (Prince, et al. 2003; Wilesmith, et al. 1988; 1991; 1992), although other routes have been considered. In fact, CFIA considered other alternatives for source of the infectious agent such as spontaneous mutation of normal prion protein to a pathogenic form and exposure to prions associated with other TSEs in its epidemiological investigations. CFIA attributed the source of animal found infected in 2003 to feed.

Based on the scientific evidence available to date, animals that have not ingested contaminated feed are unlikely to harbor the agent, so feed exposure influences risk. Animals are unlikely to have infectious levels of the agent and will present a lower risk if they were (a) born after the implementation of an effective feed ban, or (b) not fed risk material (e.g., wild animals or farmed animals that are not fed feeds containing meat-and-bone meal).

The risks associated with feed source and exposure can be mitigated by accepting for import only animals or products derived from animals that have not been fed commercial feed that is likely to be contaminated with infectious levels of the agent. If the feed ban were completely effective, this measure should be sufficient, by itself, to mitigate risk.

However, as previously mentioned, factors like unrecognized lack of compliance with the feed ban or disease transmission by alternative pathways may contribute to risk. Such risk can be mitigated further by additional risk mitigation measures. Such mitigation measures and the risk factors they are intended to address are described subsequently.

Levels of infectious agent: effect of animal age

Levels of infectious agent in certain tissues vary with the age of animal, so age of the animal influences risk. Pathogenesis studies, where tissues obtained from orally infected calves were assayed for infectivity, have shown that infectivity was not detected in most tissues until at least 32 months post-exposure (Wells, et al. 1998; Wells, et al. 1994; EU SSC 2002). The exception to this is the distal ileum, the distal portion of the small intestine, where infectivity was confirmed from experimentally infected animals as early as 6 months post-exposure.

Similar observations were made in sheep and goats (EU SSC 2002). In these animals, infectivity could not be demonstrated in the tissues until at least 16 months post-exposure to the agent.

Research demonstrates that the incubation period for BSE is apparently linked to the infectious dose received, i.e., the larger an infectious dose received, the shorter the incubation period (EU SSC 2002). While some cases have been found in animals less than 30 months of age, these have been relatively few and have occurred primarily in countries with significant levels of circulating infectivity. Specifically, BSE has been found in animals less than 30 months of age in the UK in the late 1980's to early 1990's, when the incidence of BSE was extremely high. This research also suggests that a calf must receive an oral dose of 100 grams of infected brain material containing high levels of the infectious agent to produce disease within a minimum of approximately 30 months (EU SSC 2002; DEFRA 2003; EC 2002, 2003).

BSE testing in the European Union (EU) was conducted throughout the year 2001. This testing revealed only two positive animals that were younger than 30 months of age in a total of 2,147 positive cases. Of note is that these animals were 28 and 29 months of age. For reference, in 2001, a total of 8,516,227 tests were conducted within the EU, and, of those, 1,366,243 tests were conducted on animals less than 30 months of age. In 2002, there were no animals less than 30 months of age that were positive in the EU testing scheme. Approximately 10.2 million tests were conducted in EU Member States in 2002, and, of these, 1.6 million were conducted on animals less than 30 months of age. The average mean age of positive animals in the EU in 2002 was 96.9 months, an increase from 85.9 months in 2001 (EC 2002, 2003).

This suggests a useful dividing line for purposes of mitigating risk. Infected cattle over 30 months of age or sheep and goats over 16 months of age may have levels of the abnormal prion in affected tissues that are sufficient to infect other animals fed protein derived from these tissues. Infected cattle younger than 30 months of age or sheep and

goats less than 16 months of age are unlikely to have infectious levels of the prion protein (EU SSC 2002; Wells, et al. 1994; Wells, et al. 1998). The 30 month age limit is accepted internationally in BSE standards set by various countries and is consistent with OIE recommendations (OIE 2002a).

The risks associated with age can be mitigated by accepting for import only animals or commodities derived from animals of an age where even high risk tissues are unlikely to have infectious levels of the agent. However, restrictions applicable to age alone may not be sufficient. In this regard, there are circumstances in which the age of the animal is unknown. A case in point is wild cervids. Since age can not be used to mitigate risk from these animals, alternative risk mitigation measures, which will be described subsequently, are justified. There are also circumstances in which restricting age of animal imported or source animal for a product to a particular age for a given species may not be sufficient to mitigate risk. A case in point is the requirement for removal of intestine from cattle, even those that are less than 30 months of age, the rationale for which is discussed subsequently.

Tissue localization

Some bovine tissues have demonstrated infectivity, whereas others have not (Wells, et al. 1994; Wells, et al. 1998; Wrathall, et al. 2002). Tissues that have confirmed infectivity, and thus are likely to contain the infectious agent in infected cattle, are brain, tonsil, spinal cord, eyes, trigeminal ganglia, dorsal root ganglia, and distal ileum. Affiliated tissues or structures such as skull or vertebral column are considered risk materials because of the difficulty in separating out small tissues such as dorsal root ganglia from the vertebral column.

Possibilities for cross contamination from risk materials must also be considered. For example, tonsils are directly and tightly attached to tongues, so removal of tonsil from tongues should mitigate risk. Similarly, distal ileum is a part of the intestine so removal of intestine should mitigate risk associated with infectious agent localization in the distal ileum. However, even cattle carrying the infectious agent are unlikely to carry that agent in tissues that have not had demonstrated infectivity (e.g., muscle, liver, skin, hide, milk, embryos) or products derived from these tissues (Wells, et al. 1994; Wells, et al. 1998; Wrathall, et al. 2002).

The risks associated with tissue localization can be mitigated by accepting only tissues that are unlikely to have infectious levels of the agent or commodities derived from those organs or tissues. Alternatively or in addition, if justified, risk materials can be removed. Of note in this regard is that while muscle (meat) from cattle is not, by itself, a risk tissue, it can be contaminated with vertebral column or spinal cord, and intestines from cattle younger than 30 months of age (i.e., as early as six months of age) may have infectious levels of the agent. Therefore, removal of intestine in order to remove the distal ileum from cattle less than 30 months of age is justified to mitigate risk.

Source species

Tissue distribution of the agent varies with species. No natural infections with BSE have yet been confirmed in sheep, although testing is ongoing in Europe. However, results from experimental infections of sheep have shown that the BSE prion is distributed more widely in sheep tissues than in cattle (Foster, et al. 1996; Foster, et al. 2001). This distribution is similar to the distribution of scrapie infections in sheep. In scrapie, the agent may be found in the lymphoreticular system and in peripheral nerves (Foster, et al. 1996; Foster, et al. 2001). It is assumed, based on analogy with scrapie, that, if it infected sheep naturally, BSE would distribute similarly.

Similarly, no natural infections with BSE have been confirmed in goats, although actual experiments have not been conducted in the species. In the absence of actual data, assuming that the agent did infect goats, distribution of the agent in goat tissues has been assumed to be similar to distribution of the agent in sheep tissues because of the overall species similarities.

Similarly, natural infection with BSE of cervids (deer and elk species) has not been documented, and no challenge studies on cervine susceptibility have been conducted. In the absence of experimental data, distribution of the infectious agent in cervids (if it were to infect cervids) is assumed to be similar to the distribution of CWD, a naturally occurring TSE in cervids.

Risks associated with differences in tissue distribution among species can be mitigated by accepting only tissues which are unlikely to have infectious levels of the agent or commodities derived from those tissues. These tissues may differ with species of origin because of differences in tissue localization among species. Although the tissue distribution of the TSEs in these species may be wider than in cattle, no specific risk tissues have been identified that justify removal in sheep, goats or cervids from Canada.

Prevalence of disease in region of origin

The possible prevalence of disease in the region of origin will influence the risk. Prevalence of disease will be lower in a country with adequate prevention and control measures; thus animals from such a region will be at lower risk of being exposed to infection.

The risks associated with prevalence can be mitigated by accepting commodities only from a country with a low prevalence, such as one that that can be considered minimal risk.

Potential for contamination at slaughter

There may be risks associated with contamination through processing. For example, certain tissues derived from animals killed by air injection stunning or processed using mechanically separated meat recovery systems may contain emboli or fragments from high risk tissues like brain and spinal cord, posing risk by contamination (Garland, Bauer, and Bailey 1996; Grandin 1997; Anil, et al. 1999).

Potential for mixing or inappropriate diversion

High and low risk commodities might be mixed and diverted inappropriately in slaughter facilities in which commingling is allowed. Similarly, animals from a single source, such as Canada, might be separated and diverted inappropriately if the vehicles are not sealed.

Vertical transmission

Vertical transmission (i.e., maternal transmission) may occur (Prince 2003; Wilesmith 1997; Donnelly 1997); however, experimental evidence suggests that maternal transmission is not a significant pathway for disease transmission so it will not be factored into the risk assessment.

Mitigations

Various mitigations have been applied to reduce BSE risk of spread (e.g., feed bans) and introduction into a region (e.g., restrictions defined in import certifications). The rationale by which VS has applied these mitigations to animals and products is explained. Some of the mitigations may appear to be applied in a relatively conservative fashion. By applying multiple risk mitigation measures for specified commodities, VS intends to address the potential for multiple risk factors to be associated with the commodity. However, VS feels that this approach is justified in view of the lack of precise data concerning many of the risks associated with BSE.

Feed bans

Feed bans prohibiting ruminant protein from being used in ruminant feed reduces risk of spread and amplification of the BSE agent to animals through feed by eliminating a potential source of infectious agent.

Verification and compliance

Verification by CFIA is necessary to ensure compliance with requirements for risk mitigation approaches. Verification can be provided by CFIA through endorsement of certificates that document the nature of the commodity and the risk mitigations that have been applied, inspection of facilities (e.g., dedicated or segregated slaughter facilities), review of procedures and/practices applicable to risk (e.g., feeding practices), and controlling transport conditions and route (e.g., sealing of trucks for entry through designated ports).

Contamination at slaughter

Slaughter methods that might result in contamination of low risk materials with high risk materials (e.g., air injection stunning for animals or mechanically separated meat recovery systems) can be prohibited.

Mixing or inappropriate diversion

Facilities that are dedicated to the use of low risk animals or products or in which high and low risk materials can be segregated adequately can be designated to ensure that low risk commodities are not mixed and diverted inappropriately or contaminated by high risk materials. Transport of animals from a designated origin to a designated destination in sealed vehicles can prohibit separation of the group and inappropriate diversion of animals.

Certification requirements for live animals

Certification requirements for live animals have been developed by VS to ensure that risk mitigation options are applied appropriately. These requirements, which will be defined in the proposed rule, include various forms of verification and inspection by CFIA to provide confidence that animals meet acceptable risk criteria. These standards are based on the risk considerations discussed previously and include those that follow.

VS will require certification for animals to address risks that might be presented by animal age, species, feed source, feed exposure, movement conditions, and contamination at slaughter:

- *Animals are less than a certain age*. Animals that are young enough to be unlikely have infectious levels of the agent include cattle that are less than 30 months of age and veal calves (generally defined by industry standards as less than 36 weeks of age). Also, because of their age, sheep and goats, which are defined by industry standards as less than 12 months of age would be unlikely to have infectious levels of the agent;
- *Animals are born after a feed ban was implemented.* Animals that were born after a feed ban was implemented are unlikely to be exposed to the infectious agent;

- *Animals are not known to have been fed ruminant proteins.* Animals born before a feed ban was implemented, but which were not fed risk material, are unlikely to have been exposed to the infectious agent. Animals unlikely to have been fed risk materials or exposed to the agent include wild ruminants that have not been maintained on ranches or farms. Other animals in this class include domestic ruminants fed solely on materials that are unlikely to contain the infectious agent;
- *Animal transport is controlled*. (1) Animals enter the United States through designated border crossings. Identification of designated entry points can provide control of animal movement flow and a control point where inspectors may check certifications, and, potentially, facilitate traceback, should that be necessary, and (2) Animals are transported in trucks sealed at the port of entry and the transport conditions are verified at the destination by U.S. authorities.
- *Animals are moved as a group.* Movement of animals as a group serves to maintain the identity of the shipment and ensure arrival at the intended destination for appropriate processing.

Certification requirements for products

VS will require certification for products to verify that the products originate from low risk sources and/or that high risk materials are either not present or have been removed. Certification requirements address organ or tissue localization, species differences, intended use, slaughter method, and cross-contamination, and include the following:

- Potentially high risk materials (e.g., intestine containing distal ileum for cattle) are removed during processing, so the product is unlikely to contain the infectious agent;
- The tissue being exported is not likely to contain the infectious agent (e.g., liver);
- The tissue being exported is derived from an animal that is unlikely to contain infectious levels of the agent (e.g., meat from bovids less than 30 months of age or sheep and goats less than 12 months of age).
- Possibilities for cross-contamination are minimized. For example, for bovids, the slaughter plant operates in such a manner as to prevent commingling with potentially infectious materials by being dedicated to processing of animals less than 30 months of age; processing lines for commodities are segregated so as to prevent contact between high and low risk material; or plants are dedicated to use for materials that are eligible for export to the United States;
- Product is intended for industrial applications or personal use/display (e.g., trophies). This reduces the likelihood that the product will enter the animal food chain;
- Verification by CFIA inspection ensures that various conditions meet established criteria;
- Inspection of products and approval of processes and facilities is performed in the United States. Such approvals include inspection to ensure that intestines are removed from Canadian cattle slaughtered in the United States by personnel from

the Food Safety and Inspection Service (FSIS).

Commodities under consideration for importation from Canada

VS considered the likelihood that various animals and animal products might have infectious levels of the agent. Since this analysis focuses on risk originating from Canada, the commodities discussed reflect animals and products that were being imported into the United States from Canada prior to the ban, and, for which trade may be reinitiated.

Risk considerations for individual commodities are grouped as live ruminants (Table 1) or ruminant products (Table 2) from minimal risk regions. The information is presented in tabular form. Listed in the first column of the table are individual commodities. The second column contains mitigations that APHIS intends to apply. The third column contains a summary of the mitigations affecting the likelihood that the commodity will contain infectious levels of the agent, including factors relating to the nature of the commodity (e.g., age of animal, tissue of origin) and external mitigations that APHIS will require (e.g., feed source, verification).

Risk considerations are discussed and mitigations to address that risk are assigned to animals and animal products that might be imported from Canada. The mitigations assigned to individual commodities were based on extensive discussion of the risk factors and mitigations described previously in this document and a consideration of the likelihood that the material might contain infectious levels of the BSE agent.

Risk deliberations were undertaken by a permanent technical advisory team of experts within APHIS, the TSE Working Group. This group is composed of 13 members, one or two from each of the following APHIS units: Centers for Epidemiology and Animal Health, National Veterinary Services Laboratories, National Center for Animal Health Programs, VS Regional Offices, Center for Veterinary Biologics, National Center for Import and Export, Plant Protection and Quarantine, and Legislative and Public Affairs. The group was formed several years ago to address and make policy recommendations regarding issues associated with TSEs.

Live animals from minimal risk regions

The technical group applied the general considerations listed in bullet form in assigning mitigations to live animals (Table 1). Specific considerations applied to each commodity are identified in the table.

Risk from

- Bovids less than 30 months of age intended for immediate slaughter is mitigated primarily by restrictions on age, feed source, movement controls, and removal of risk materials. With regard to age, it is unlikely that animals that are less than 30 months of age have infectious levels of the agent in most tissues. This applies not

only to cattle but also to veal calves less than 36 weeks of age and sheep and goats less than 12 months of age;

- Bovids for feeding is also mitigated by restrictions on feed source, removal of risk tissue, and movement (e.g., to designated feedlot, through specific ports of entry). In addition, since the animals will reside in the United States until slaughter they are identified as Canadian in origin by tattoo. Age is addressed by the requirement that they be slaughtered before they reach 30 months of age;
- Animals can be mitigated by limiting imports to animals that have not been fed ruminant proteins (other than milk protein) or, where there is not a maximum age at which the animals might be slaughtered, that were born after the feed ban or removing risk materials;
- Sheep or goats less than 12 months of age are considered to be mitigated by age restrictions because (a) there is no known natural infection with BSE of sheep and goats, and (b) although the species can be infected with the BSE agent experimentally, infectious levels of the agent have only been found in animals older than 16 months. Other mitigations are generally consistent with those for bovids;
- Cervids is mitigated by restricting imports to wild animals that are unlikely to have been exposed to contaminated feed or requiring that CFIA exercise oversight of feeding practices and potential for occurrence of TSE. For live animals, oversight of feeding practices is addressed by CFIA documented certification that the herd is one in which surveillance is conducted according to national or provincial standards by appropriate authorities. The herd is not known to be affected with or exposed to a TSE. At present, the TSE program for cervids in Canada is one that monitors for CWD. However, all sampling done to monitor for CWD would identify animals that might be affected with other TSEs such as BSE. This requirement provides assurance and verifies that CFIA is monitoring for TSE diseases, in general, and that there is no evidence of other TSE;
- Tissues of animals of any species can be mitigated by requiring that risk materials (e.g., intestine in bovids) are removed, either in the United States under FSIS supervision, or in Canada with CFIA certification. Because of evidence the infectious levels of the BSE agent may be present in the distal ileum of infected bovids as early as 6 months post-exposure, removal of intestines in a manner considered adequate to ensure that the materials are not fed to ruminants should further mitigate risk of cattle less than 30 months of age. No specific risk tissues have been identified that justify removal from sheep, goats, or cervids;
- Animals of any species can be mitigated by maintaining identity and controlling movement, e.g., requiring trucks to be sealed, entry to be through designated ports, shipments to be adequately documented with appropriate forms, animals to be moved as a group, movement to be directed to a designated destination, and animal origin to be identified (e.g., by tattoo). Movement of animals as a group is particularly relevant to movement of animals to a feedlot or to slaughter. Animals going to slaughter are moved and slaughtered as a group to maintain identity to ensure that their intestines are removed. Animals going to feedlots are identified by tattoo to insure that their identity is not lost at the feedlot and to ensure that

their intestines are removed at slaughter;

- Animals of any species can be mitigated by requiring CFIA to certify or verify that the conditions are appropriate for the commodity;
- Diversion of animals going direct to slaughter, for which a health certificate is not required (APHIS 2004f), is mitigated by requirement that truck be sealed and the contents documented direct to slaughter to be opened under supervised conditions.

Table 1 - Live animals from minimal risk regions

Commodity Description	Required Risk Mitigations	Risk factor/mitigation summary
Bovids imported for slaughter by 30 months of age, including veal calves (intended for immediate slaughter)	Trucks are sealed and contents documented to move direct to slaughter as a group; CFIA verifies that the animals were under 30 months of age and not known to have been fed ruminant proteins during their lifetime; intestine is removed at U.S. plant under FSIS supervision and disposed of appropriately; animals enter United States through VS designated ports of entry.	Source is young animals not known to have been fed ruminant proteins; CFIA and FSIS verify; risk materials are removed; movement is controlled.
Bovids imported for feeding in a U.S. feedlot prior to slaughter by 30 months of age or less.	CFIA verifies that the animals are less than 30 months of age and are not known to have been fed ruminant protein during their lifetime; animals must be moved to designated feedlot as a group and slaughter at less than 30 months of age; intestine is removed at U.S. plant under FSIS supervision and disposed of appropriately; cattle come in through VS designated ports of entry; ear tattoo identifies them as Canadian in origin.	Source is young animals not known to have been fed ruminant proteins; feedlot is designated; movement to feedlot is controlled; CFIA and FSIS verify; risk materials are removed; animals are identified as Canadian.
Sheep or goats imported for slaughter by 12	Trucks are sealed and contents documented to	Source is young animals not known to have been fed

months of age (intended for immediate slaughter)	move direct to slaughter as a group; CFIA verifies that the animals were under 12 months of age and are not known to have been fed ruminant proteins during their lifetime; animals enter United States through VS designated ports of entry.	ruminant proteins; CFIA verifies; movement is controlled;
Sheep and goats imported for feeding in a U.S. feedlot prior to slaughter by 12 months of age or less	CFIA verifies that the animals are under 12 months of age and are not known to have been fed ruminant protein during their lifetime; animals must be moved as a group to designated feedlot and to slaughter at less than 12 months of age; animals come through VS designated ports of entry; ear tattoo identifies them Canadian in origin.	Source is young animals not known to have been fed ruminant proteins; feedlot is designated; movement to feedlot is controlled; CFIA and FSIS verify; animals are identified as Canadian.
Cervids (intended for immediate slaughter)	Trucks are sealed and contents documented to move as a group direct to slaughter; CFIA verifies that the animals were born after the feed ban and are not known to have been fed ruminant proteins during their lifetime; cervids enter United States through designated ports of entry. Animals must be members of a herd participating in a nationally or provincially recognized TSE surveillance program; herd is not known to have been infected with or exposed to TSE.	Source is animals under surveillance for TSE, not known to have TSE, born after feed ban, and not known to have been fed ruminant proteins; CFIA verifies; movement is controlled.

Ruminant products from minimal risk regions

The technical group applied the general considerations listed in bullet form in assigning mitigations to ruminant products (Table 2). Specific considerations applied to each commodity are identified in the table.

Risk from

- Any material can be mitigated, in part, by requiring that mitigations be applied to the source animal as described for Table 1 (e.g., meat from cattle less than 30 months of age that have not been known to been fed ruminant proteins or veal from calves less than 36 weeks of age). In addition, for products, other mitigations for source animals would include requirements that they be wild animals, not farmed or ranched, that are unlikely to have been exposed to the infectious agent through feed;
- Any situation where high and low risk commodities might be mixed or improperly diverted can be mitigated by requiring that slaughter facility only kills animals less than a designated age (e.g., dedicated to bovids less than 30 months or sheep and goats less than 12 months) or complies with a facility segregation procedure approved by CFIA and endorsed by APHIS as sufficient to prohibit contamination or commingling of meat with products not eligible for importation into the United States;
- Meat can be mitigated by prohibiting processing conditions that might result in contamination (e.g., mechanically separated meat). The issue is addressed in the USDA definition of meat, which excludes mechanically separated meat or other products that contain bone or central nervous system tissue (FSIS 2003);
- Any product can be mitigated by requiring removal of relevant risk materials. For example, to ensure removal of distal ileum, intestine is removed from cattle and, because there is no age restriction for bovids constituting a source of tongues, tonsils are removed prior to export;
- Hunter harvested animals can be mitigated by requiring that the materials derived be imported only for personal use, which makes it highly unlikely that the item or its derivatives would enter the food chain for animals. Of relevance to imported materials from Canada are caribou and musk ox meat that are sold commercially after harvesting from wild animals on Nunavut lands;
- Animals in cervine herds can be mitigated by requiring them to originate from herds in which surveillance is conducted by national or provincial authorities. The herd is not known to be affected with or exposed to a TSE. In addition, surveillance for TSE in cervids is conducted according to national and/or provincial standards;
- Tallow may be mitigated by requiring that it contain less than 0.15 percent protein because tallow is primarily lipid material with a minimal cellular component. When it is derived from bovids less than 30 months of age and the level of protein is low, the material would be unlikely to contain prion protein;

Liver is mitigated because the tissue unlikely to contain the agent in animals of any age, regardless of feed source, unless the liver is contaminated as a result of air-injected stunning which often drives emboli of brain tissue into the liver; Tongues are a low risk tissue in themselves. However, they may be derived from bovids older than 30 months and may be contaminated with adjacent tonsils which may pose a risk in animals older than 30 months of age. Therefore, risk is mitigated by control of the feed source and removal of tonsils.

Table 2 - Ruminant products from minimal risk regions

Commodity Description	Required Risk Mitigations	Risk factor/mitigation summary
Bovine meat, fresh, chilled, or frozen (including veal), from animals less than 30 months of age that meets USDA definition of meat.	CFIA verifies that the animals were less than 30 months of age when slaughtered and are not known to have been fed ruminant proteins during their lifetime; slaughter plant only kills bovids less than 30 months of age or complies with a facility segregation procedure approved by CFIA and endorsed by APHIS for bovids older than 30 months of age; intestine is removed; meat processing must meet USDA standards.	Source is young animals not fed ruminant proteins; slaughter plant is segregated or dedicated to prevent commingling or diversion; intestine is removed, CFIA verifies.
Bovine whole or half carcasses from animals less than 30 months of age.	CFIA verifies that the animals were less than 30 months of age when slaughtered and are not known to have been fed ruminant proteins during their lifetime; intestine is removed at slaughter plant that only kills bovids less than 30 months of age or complies with a facility segregation procedure approved by CFIA and the Administrator.	Source is young animals not known to have been fed ruminant proteins; slaughter plant is dedicated or segregated to prevent commingling or diversion; CFIA verifies.
Fresh or frozen bovine liver	CFIA verifies that the product is pure liver and that no air-injected stunning process was used at slaughter.	Tissue of origin is not risk tissue; CFIA verifies.

Fresh or frozen bovine tongues	CFIA verifies that the animals were born after the feed ban and are not known to have been fed ruminant proteins during their lifetime; tonsils are removed.	Source is animals born after feed ban and not known to have been fed ruminant proteins; risk tissues are removed; CFIA verifies.
Sheep or goat meat, fresh or frozen, from animals under 12 months of age that meets USDA definition of meat	CFIA verifies that the animals were less than 12 months of age when slaughtered and are not known to have been fed ruminant proteins during their lifetime; slaughter plant only kills sheep or goats less than 12 months of age or complies with a facility segregation procedure approved by CFIA and the Administrator, meat processing must meet USDA standards.	Source is young animals not fed ruminant proteins; processing methods are restricted; slaughter plant is dedicated or segregated to prevent commingling or diversion; CFIA verifies.
Fresh lamb or kid carcasses	CFIA verifies that the animals were less than 12 months of age when slaughtered and were not known to have been fed ruminant proteins during their lifetime; slaughter plant only kills sheep or goats less than 12 months of age or complies with a facility segregation procedure approved by CFIA and the Administrator.	Source is young animals not known to have been fed ruminant proteins; slaughter plant is dedicated or segregated to prevent commingling or diversion; CFIA verifies.
Hunter-harvested ruminant, cervine, sheep or goat whole dressed carcass (eviscerated and the head removed) or meat of wild cervids, sheep, goats or other meat from ruminants for personal use	CFIA verifies that feeding processed feed to wildlife is not practiced in the province where the animal was harvested; hunter shows proof that animal was a legally harvested wild (not ranched) animal. Such proof will include the hunting license, tag or equivalent.	Source is wild ruminants not fed commercial processed feed; CFIA verifies; hunter verifies.

Cervine meat or other products from farmed animals (includes shooter bulls or shooter bucks) processed in a slaughterhouse; with or without bone, fresh or frozen; ground meat or sausage is allowable if it is derived from either (1) only cervine meat or (2) only cervine and non-ruminant meat	CFIA verifies that the animals were born after the feed ban and are not known to have been fed ruminant proteins during their lifetime. Animals must be members of a herd not known to be infected with or exposed to a TSE.	Source is animals born after feed ban and not fed ruminant proteins; herd not known to have TSE; CFIA verifies.
Caribou and musk ox meat from Nunavut lands, with or without bone, fresh or frozen (represents specialty commercial product derived from wild animals in the province)	CFIA verifies that feeding of processed feed to wildlife is not practiced and that meat is from wild animals harvested on Nunavut lands; that the processing facility either slaughters only cervids eligible for entry into the U.S. or complies with a facility segregation procedure approved by CFIA and the Administrator.	Source is wild ruminants not fed commercial processed feed; processing facility is dedicated; CFIA verifies.
Gelatin from bones of cattle less than 30 months of age.	CFIA verifies that source animals are less than 30 months of age that are not known to have been fed ruminant proteins.	Source is young animals not known to have been fed ruminant protein; CFIA verifies.
Tallow for unrestricted use from bovids less than 30 months of age.	CFIA verifies that the tallow is less than 0.15 percent protein and is derived only from bovids born after the feed ban, less than 30 months of age, and not known to have been fed ruminant proteins during their lifetime; intestines were removed.	Source is animals born after feed ban and not known to have been fed ruminant proteins; risk tissues are removed; animals are ambulatory; CFIA verifies.
Cervine offal (viscera or non-muscle tissues removed from a carcass at slaughter), fresh, chilled or frozen	CFIA verifies that the animals were born after the feed ban and are not known to have been fed ruminant proteins during their lifetime; animals must be members of a herd not known to be infected with or exposed to a TSE.	Source is animals born after feed ban and not known to have been fed ruminant proteins; herd is not known to be infected with TSE; CFIA verifies.

In summary, VS considers that Canada is a minimal risk region for BSE. However, in light of the recent positive animal, VS has analyzed BSE mitigations relevant to live animals and products that might be imported from Canada. These additional mitigation measures address epidemiological risk factors for disease transmission that VS has identified. VS concludes from this analysis that the requirements described in this analysis are adequate to mitigate BSE risk from Canadian imports of these products.

Based on these conclusions, and in compliance with OIE recommendations (OIE 2002b), adequate information was presented for VS to complete the risk assessment at this point. However, in the interests of thoroughness, VS continued its assessment to briefly address risk associated with exposure and consequence.

Exposure Assessment

VS considers it unlikely that infectious levels of BSE would be introduced into the U.S. from a minimal risk country like Canada with any of the commodities discussed in this assessment. Also, VS considers that, even if the BSE agent were introduced into the United States, it would be extremely unlikely to be introduced into commercial animal feed and thereby infect animals. That is a primary result of the nature of the products, none of which is likely to become a significant animal feed component.

Several specific observations are relevant in this regard. First of these is the low number of infected animals or products that might conceivably be imported into the United States from Canada, based on the low prevalence that was identified (i.e., only a single infected Canadian animal that has been identified). Second is the extremely low likelihood that an infected animal or product from an infected animal would enter the U.S. animal feed chain. Third is the extremely low likelihood that an animal or product would contain infectious levels of the agent. Fourth is the likelihood that the mitigations applied by VS would reduce the likelihood of all of the above.

These conclusions are consistent with the results of the Harvard study (Harvard Center for Risk Analysis et al. 2001). The analysts developed a probabilistic simulation model to characterize the consequences of introducing BSE into the United States. The model analyzed the effects of introducing hypothetical numbers of infected animals the United States. The model allowed predictions of the number of newly infected animals that would result from introduction of BSE, the time course of the disease following its introduction, and the potential for human exposure.

For example, in a hypothetical scenario in which ten BSE-infected cattle were imported into the United States, the results suggested that an average of only three new cases of BSE would occur. These cases would occur primarily as a result of non-compliance with the feed ban. In the unlikely event that disease was introduced, it would be almost certain to be eliminated within 20 years under the conditions currently existing in the United States.

Reducing the hypothetical number of infected animals imported to one resulted in an estimate of less than one new BSE case in 20 years.

Of note in relation to the scenarios tested in the study is the hypothesis that one or ten animals are imported to the United States from Canada. In fact, there is no evidence to date that any infected animals have been imported, and only a single indigenous case of BSE has been detected in all of Canada, despite extensive surveillance and traceback efforts.

In summary, the scenarios presented in the Harvard study (Harvard Center for Risk Analysis 2001) assess the likelihood of BSE spread upon the unlikely event that it was introduced into the United States. The study results suggested that, should BSE be introduced, the disease is extremely unlikely to become established in the United States. Any new cases of BSE would be most likely a result of lack of compliance with the regulations enacted to protect animal feed.

The study concluded that the most effective U.S. measure preventing BSE spread is the feed ban instituted by the Food and Drug Administration (FDA) in 1997 (DHHS) to prevent recycling of potentially infectious cattle tissues. The FDA feed ban greatly reduces the chance that BSE will spread from a sick animal to other cattle through feed.

In summary, the fact that Canada has detected only a single indigenous case of BSE, the strong BSE controls Canada has in place, and the importation restrictions VS would impose before allowing these imports make it unlikely that BSE would be introduced from Canada. Additionally, the Harvard study suggested that the measures taken by the U.S. government and industry make the United States robust against the spread of BSE toanimals should it be introduced into this country. These measures, which include ensuring compliance with the FDA feed ban and reducing the potential for infectious tissues to enter the animal food supply will ensure that these risks remain low.

Thus, considering all available data and scientific information, VS considers exposure risk to the agent to be low.

Consequence Assessment:

A consequence assessment describes the consequences of introduction of BSE into the United States. This consequence assessment addresses both direct and indirect consequences as recommended by the OIE (OIE 2002b). Direct consequences include animal infection, disease and production losses, and public health consequences. Indirect consequences include surveillance and control costs, compensation costs, potential trade losses, and adverse consequences to the environment.

Animal health

BSE is unlikely to have a major direct influence on animal health at the national level. Although the disease is devastating to the individual animal and its ultimate effect is death, it is very unlikely, based on the single occurrence of BSE in Canada, that a significant number of infected animals would be imported into the United States from Canada. If any infected animals did enter, the disease would be unlikely to spread to others and, essentially the infected animals should constitute dead end hosts.

Public health

As previously mentioned, although public health consequences are not issues under the regulatory authority of APHIS, we address the issue in this assessment. The primary public health consequences would appear as occurrences of variant Creutzfelt-Jacob Disease (vCJD), a neurological disorder in humans apparently associated with ingestion of BSE-contaminated meat products. Although there are many unknown factors relative to development of vCJD, including the definition of an infectious dose or the length of an incubation period, of significance to this analysis is that the available information compiled from a variety of studies suggests the infectious agent may be 10 to 100,000 times less pathogenic in humans than in cattle (summarized in Harvard Center for Risk Analysis 2001; EUSSC 2000).

Risk of such public health consequences should be extremely low in the context of importation of BSE infected commodities from Canada. The Harvard study found that even if BSE were to enter the United States, it would be unlikely to spread. Therefore, it would be unlikely to enter the human food chain. Third, is the extremely low likelihood that, should an infected carcass enter the food chain, the tissues that present the highest risk of infection would be available for human consumption. The Harvard study demonstrated that, even if BSE were to occur in the United States, little infectivity would be available for potential human exposure.

Surveillance, control, and indemnity

An Interagency Working Group formed by the Secretary of Agriculture issued a report on risks and economic impacts associated with the potential introduction of BSE into the United States (USDA 2002). In addition to the other costs, a BSE occurrence in the United States would cause economic costs due directly to costs of the government response to the disease. This would include both direct losses to BSE and depopulation of contact herds. A single case would be likely to necessitate the depopulation of several thousand animals along with associated indemnity costs. Additional costs would be incurred for surveillance, testing, and disposal of carcasses. Multiple cases could cause the loss of a substantial portion of the U.S. herd. Furthermore, the cost of the investigation into the source and causes of the incident could require large government expenditures. The report concluded that the response would depend on the nature of the outbreak, and, as such, the costs of such a program are difficult to predict.

Information relevant to potential costs to the U.S. government may be provided by the Canadian experience. VS presents data from the Canadian experience with BSE, which we believe reflects the type of scenario most likely to constitute a model for any experience the United States might have. In this regard, the Canadian experience reflects expenditures incurred as a result of BSE detection in a single animal, not the widespread disease that was observed in Europe (CFIA 2003b). Specifically, as of August 31, 2003, CFIA documented expenditures related to animal infection, disease, production losses, and surveillance and control costs of approximately $5.7 million (Canadian dollars) on salaries, $1.4 million on costs other than salaries, and $7.0 million on indemnities. The total estimated costs of BSE detection and the CFIA response in Canada were $14 million Canadian dollars, which is equivalent to approximately $19 million U.S. dollars. For reference, there are approximately 45 million adult cattle in the United States (USDA-NASS) in comparison to approximately 5.5 million in Canada (CFIA 2003a).

Effects on trade

Trade-related economic consequences of a BSE introduction from Canada would result if other countries refused to accept U.S. ruminant products. Again, the Canadian experience provides relevant information on trade consequences. In this regard, the United States could expect the spectrum of trading partners imposing restrictions on the U.S. because of BSE to be similar to the countries imposing restrictions on Canada. As of August 11, 2003, 49 countries had imposed restrictions on Canadian animals and products as a result of the BSE-infected animal.

Countries imposing restrictions on Canada included Japan, Mexico, and Korea (CFIA 2003). These three countries also constitute major U.S. export markets. The value of lost exports to these three U.S. ruminant markets alone would total $3 billion annually if trade restrictions were enforced against the United States: Japan ($1.2 billion); Mexico ($1.12 billion); and South Korea ($712 million). Indirect economic losses to U.S. firms that support ruminant exports to these three markets would equal an additional $2.5 billion annually. The magnitude of these values reflects both animal and product exports (Green and Grannis 2003).

More than 33 thousand full-time U.S. jobs, accounting for almost $1 billion in wages annually, could be jeopardized by loss of these three markets. In the longer term, if trade restrictions persisted and alternative export markets did not develop, the U.S. ruminant production sector could contract, allowing other supplying countries to establish trade relationships in the absence of U.S. supply (Green and Grannis 2003).

Effects on the environment

Environmental effects have been considered under all applicable environmental review laws in force in the United States. These are considered in a separate, but related, environmental assessment (APHIS 2003d). The environmental assessment was conducted in compliance with the National Environmental Policy Act and

implementing regulations (NEPA 1969).

Risk Estimation

VS concludes from this assessment that the surveillance, prevention, and control measures implemented by Canada are sufficient to minimize the risk of importing BSE into the United States, provided that additional mitigation measures are implemented as described. Furthermore, VS concludes that the animals and animal products under consideration in this analysis are of low or minimal risk in view of the certification requirements that will be implemented.

These conclusions are consistent with the 2001 Harvard study, which found that the measures taken by the U.S. government and industry make the United States robust against the spread of BSE, should it be introduced into the country. Of particular significance in this regard is the feed ban instituted by the FDA in 1997 to prevent the recycling of potentially infectious ruminant tissues (DHHS).

VS concluded from the consequence assessment that the consequences with regard to animal health, human health, and the environment were minimal or low. The major economic consequence of importing a BSE infected animal would be trade losses. Although these would be significant, it is important to note that the results of both the release and exposure assessment indicated that the risk of introduction and establishment of BSE was low.

In summary, VS considers the risk of BSE-imported animals or animal products entering the United States from Canada and exposing U.S. livestock through feeding of infected materials to susceptible animals, to be low.

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Appendix 2: Explanatory Note:

Risk Analysis: BSE Risk from Importation of Designated Ruminants and Ruminant Products from Canada into the United States

Animal and Plant Health Inspection Service

Veterinary Services

February 2004

Appendix 2: Explanatory Note: Risk Analysis: BSE Risk from Importation of Designated Ruminants and Ruminant Products from Canada into the United States; Animal and Plant Health Inspection Service, Veterinary Services, February 2004

Introduction and Objective

On November 4, 2003, the U.S. Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) published a risk analysis and proposed rule (Federal Register, Vol. 68, No. 213, pp. 62386-62405) which defined a new category of minimal risk regions for bovine spongiform encephalopathy (BSE), proposed to classify Canada as such a region and defined risk mitigations that it would apply to imports of ruminants and ruminant products from Canada. APHIS determined that this action was warranted because it would continue to protect against the introduction of BSE into the United States while removing unnecessary prohibitions on certain commodities from Canada and other regions that qualify as BSE minimal-risk regions. At the time, BSE had never been detected in the United States, and only a single indigenous case had been reported in Canada.

On December 23, 2003, USDA announced a presumptive positive case of BSE in a Holstein cow that was slaughtered in the State of Washington. The epidemiological investigation revealed that the animal was born in Canada and most likely exposed to the BSE agent in that country. This imported case was detected after USDA published its risk analysis and proposed rule. The question has been raised as to whether the results of the risk analysis were altered by the finding of this infected animal.

This document explains why the detection of the BSE-infected cow in the United States does not affect the conclusions of the risk analysis. Although each component of the risk analysis will be addressed (release, exposure, consequence, and risk estimation), the detailed discussion presented in the original analysis will not be repeated. Rather, this note will explain the relevance of the new information to each component. It will also summarize control mechanisms in place at the time of the incident and new initiatives taken subsequently.

Background

The infected cow entered the United States on September 4, 2001, as part of a shipment of 81 animals from the source herd in Canada. The USDA has conducted an intensive epidemiological investigation, details of which are provided in the enclosure. The results indicated that the animal was born, and most likely became infected, in Alberta, Canada. Risk animals in the United States were traced and culled according to international standards; no additional cases were identified.
The epidemiological investigation revealed several points that are relevant to this explanatory note:

- The cow was approximately 6 years and 8 months old at the time the disease was diagnosed. Its age indicated that it was born prior to the implementation of the feed ban in Canada. Therefore, it was most likely to have become infected prior to the implementation of the feed ban in that country.

- The animal was imported in 2001 at approximately 4 1/2 years of age.

Release assessment

The risk analysis that was published in October 2003 evaluated the risk of importing BSE-infected animals and animal products from Canada under the restrictions described in the risk analysis and proposed in the rule. Included among these were restrictions that prohibited importation of animals older than 30 months of age and animals that had been fed ruminant protein.

The risk analysis addressed the likelihood that animals might have been infected prior to the implementation of the feed ban in Canada. It noted that the feed ban took effect in August 1997 and that compliance with the feed ban appeared to be good. In addition, the document cited evidence to indicate that the animals most likely to have infectious levels of the agent were 30 months of age or older.

Both of the BSE cases of Canadian origin occurred in cattle born before the feed ban was implemented. They were both older than 30 months of age when they were diagnosed as infected. Infection presumably occurred prior to or around the time the Canadian feed ban was enacted. The finding of an imported case in a cow greater than 30 months of age has little relevance to an analysis of risk under the proposed mitigation measures, beyond the implications for BSE prevalence in Canada. The proposed rule was not in effect in 2001 when the imported case, which was more than 4 years old at the time, entered the United States. Under the proposed conditions, the animal would not have been allowed entry into the United States. Therefore, we continue to consider the import controls in the proposed rule to be effective and the results of the analysis unchanged.

With regard to BSE prevalence in Canada, APHIS presented evidence in the original risk analysis that the prevalence was very low and that Canada had strong BSE controls in place. Although an additional animal of Canadian origin has been diagnosed with BSE since APHIS published its risk analysis and proposed rule, the total number of diagnosed cases attributed to that country remains low. Furthermore, Canada has implemented strong measures to prevent the establishment, propagation and spread of BSE among cattle; to detect infected animals through its surveillance program; and to protect the animal and human food supplies.

Consequently, it remains unlikely that BSE would be introduced from Canada under the conditions described in the proposed rule. Based on factors discussed in the original risk analysis and the existing and proposed risk mitigation measures, APHIS concludes that an additional BSE case of Canadian origin does not significantly alter the original risk estimate.

Exposure assessment

Actions being taken in the United States

Despite the fact that detection of the infected animal did not influence the original risk conclusions, it did raise consciousness of BSE challenges that might exist for the United States. As a result, the United States is redirecting resources toward planning, implementation, and enforcement of national policy measures to enhance BSE surveillance and protect human and animal health. Towards this end, an international panel of scientific experts appointed by the Secretary of Agriculture has provided a review of U.S. BSE response actions and made recommendations for enhancements of our national program. A copy of the report is available at http://www.aphis.usda.gov/lpa/issues/bse/bse.html.

The expert panel was complimentary of the scope, thoroughness and appropriateness of the epidemiological investigation and concluded that the investigation conformed to international standards. Key policy recommendations included (1) incorporation of multiple redundancies in production systems to prevent inclusion of specified risk materials (SRMs) in human food and animal feed, and to avoid cross-contamination; (2) additional measures to ensure continued access to nonambulatory cattle for surveillance purposes and to prevent them from entering into the food and feed chains; (3) enhanced targeted and passive BSE surveillance systems; (4) improved traceability through a comprehensive national animal identification system; and (5) reinforced educational efforts.

APHIS is evaluating these recommendations, many of which build on actions already taken in the United States, and considering policy options. However, APHIS believes that the recent detection and investigation of the single imported BSE case demonstrates the effective nature of the surveillance and response measures currently in place. Relevant to this, the expert panel did not expressly consider the measures implemented since 1985 to reduce the threat of BSE exposure or amplification within the United States. The U.S. Government has already taken significant actions that directly address many of the expert panel recommendations. Those actions are summarized in the following discussion.

The previous risk analysis identified the feed ban as the most effective risk mitigation measure for BSE. The United States implemented a feed ban prohibiting the use of most mammalian protein in feeds for ruminant animals which became effective on August 4, 1997. The rule establishing the feed ban was implemented by the U.S. Department of Health and Human Services' (HHS) Food and Drug Administration (FDA) and appears in Title 21, *Code of Federal Regulations*, Part 589.2000. Current estimates of compliance with the ban exceed 99 percent.

More recently, both USDA and FDA have initiated food and feed safety measures in response to the detection of the imported BSE case. General information and links to relevant documents are available at http://www.fsis.usda.gov/oa/news/2004/bseregs.htm.

For example, the feed ban, although comprehensive, currently allows nonruminant protein in ruminant feeds. FDA has announced the future publication of an interim final rule designed to further minimize the risk that cattle will be purposefully or inadvertently fed prohibited protein. Details of this announcement are available on the HHS' Web site at: http://www.hhs.gov/news/press/2004pres/20040126.html. The anticipated regulations will eliminate the exemption in the 1997 feed rule that allows mammalian blood and blood products to be fed to other ruminants. It will also ban the use of "poultry litter" and "plate waste" as feed ingredients for ruminants. The interim final rule will also minimize the possibility of cross-contamination of ruminant and nonruminant feed by requiring equipment, facilities, or production lines to be dedicated to nonruminant animal feeds if they use protein that is prohibited in ruminant feed.

To ensure continuing compliance with the new measures, in 2004, FDA has announced its intention to expand the scope of its inspections of feed mills and renderers. FDA will itself conduct 2,800 inspections and will continue to work with State agencies to fund 3,100 contract inspections of feed mills, renderers, and other firms that handle animal feed and feed ingredients. Through partnership with State agencies, FDA will also receive data on 700 additional inspections, which will account for 100 percent of all known renderers and feed mills that process products containing materials prohibited in ruminant feed.

In addition, FDA has begun a feed sampling program and is continuing to support the development and evaluation of diagnostic tests to identify prohibited materials. These tests would offer a quick and reliable method of testing animal feed for prohibited materials.

USDA has responded to the imported BSE case with significant risk mitigation measures as well. Perhaps most importantly, SRMs, the tissues that are most likely to contain the infectious agent, are banned from the human food supply. On January 12, 2004, USDA's Food Safety and Inspection Service (FSIS) published an interim final rule in the *Federal Register* (the official publication of U.S. Government regulations) that established as SRM the skull, brain, trigeminal ganglia, eyes, vertebral column, spinal cord, and dorsal root ganglia of cattle over 30 months of age, as well as the tonsils and small intestine of cattle of all ages. This regulation was effective immediately upon publication and prohibits the use of these materials in the human food supply.

Since identification of animal age is important to enforcement of this rule, FSIS has also developed procedures for verifying the age of cattle that are slaughtered in official establishments by examination of dentition. These measures are consistent with the actions taken by Canada after the discovery of BSE in that country in May 2003.

Disposal of SRMs has been identified as an issue that should be addressed. Through the interim final rule described above, FSIS further requires federally inspected establishments that slaughter cattle to develop, implement, and maintain procedures to remove, segregate, and dispose of these SRMs so that they cannot enter the food chain. Slaughter plants must also make that information readily available for review by FSIS inspection personnel. Plants inspected by State officials must have procedures in place that are equivalent to the new Federal requirements.

Since mechanically separated meat may be contaminated with SRMs during the separation process, the interim final rule on SRMs also prohibits the use of mechanically separated meat in human food.

FSIS has also taken actions that will effectively prohibit use of advanced meat recovery (AMR) in meat production from cattle that are 30 months of age or older.[1] In this regard, FSIS previously had regulations in place that prohibit spinal cord from being included in boneless meat. However, a new regulation, effective upon publication in the *Federal Register* on January 12, 2004, expands that prohibition to include dorsal root ganglia (clusters of nerve tissue connected to the spinal cord along the vertebral column), which could potentially be incorporated into boneless meat products through AMR. In addition, because the vertebral column and skull in cattle 30 months of age and older will be considered inedible, they cannot be used for AMR. Air injected stunning, a process for humanely stunning cattle for slaughter, has been identified as a process that may result in contamination of carcasses with brain tissue. To ensure that portions of the brain are not dislocated into the tissue of the carcass as a result of the process, FSIS banned the practice of air-injection stunning with the publication of an interim final rule in the *Federal Register* published on January 12, 2004. Of note is the fact that industry had already voluntarily implemented a ban on air-injection stunning. Screening for SRMs and verification of their absence in products has been identified as an issue that should be addressed. Therefore, in March 2003, FSIS began a routine regulatory sampling program for beef produced from AMR systems to ensure that spinal cord tissue is not present in the product. In the new interim rule, establishments must ensure process control through verification testing to ensure that neither spinal cord nor dorsal root ganglia is present in the product.

Before detection of the imported BSE-infected animal, certain downer cows were permitted to enter the human food supply. However, that will no longer be allowed. Effective on December 30, 2003, the USDA excluded all nonambulatory cattle from the human food chain. The specific details of this prohibition are established in the interim rule on SRM published in the *Federal Register* on January 12, 2004. All non-ambulatory animals, regardless of the reason for their nonambulatory status or the time at which they became nonambulatory, will be condemned at slaughter and prevented from entering the

[1] AMR is an industrial technology that removes muscle tissues from the bone of beef carcasses under high pressure without incorporating bone material when operated properly. AMR enables processors to remove small amounts of meat from carcasses without breaking bones, but concerns have been raised regarding potential contamination of the meat with central nervous system tissue.

human food supply. In addition, FDA has extended that action and announced the future publication of an interim final rule that bans any material from nonambulatory (downer) or dead cattle, as well as SRM and mechanically separated beef, from FDA-regulated human food, including dietary supplements and cosmetics. To further control the incorporation of material from nonambulatory cattle in human food, an interpretive rule published in the *Federal Register* on January 12, 2004, mandated that FSIS inspectors not mark cattle tested for BSE as "inspected and passed" until confirmation is received that the animals have, in fact, tested negative for BSE.

Surveillance activities are being enhanced beyond the active targeted surveillance program for BSE that has been in place in the United States since May 1990. Since inception of the program, the United States has targeted at-risk populations and has steadily increased the number of cattle tested. This approach is fully consistent with standards set out by the Office International des Epizooties (OIE).

USDA intends to maintain the focus of its surveillance efforts on nonambulatory cattle as it has in the past since this is a high risk target population. Concerns have been raised that access to nonambulatory animals as a target population for surveillance may be less than optimal if the animals are not sent to slaughter. Therefore, USDA is considering options to ensure continued access to nonambulatory animals. Relevant to this, even prior to the announcement on December 30, 2003, that a BSE-infected cow had been detected in the United States, not all nonambulatory cattle went to FSIS-inspected slaughter facilities. APHIS had already established efforts to sample this population at other salvage or rendering facilities and will continue to work closely with components of the animal disposal industry to ensure continued surveillance of these animals, as well as appropriate disposal. USDA will also increase efforts to obtain more samples from this high-risk group on the farm.

USDA is working to enhance its BSE testing capacity. Currently, all of the testing conducted as part of the U.S. surveillance program for BSE is currently performed by APHIS at the National Veterinary Services Laboratories (NVSL) in Ames, Iowa. NVSL personnel are evaluating more rapid assays, and APHIS is accepting data submissions to support licensing these tests. One of the ELISA tests (BioRad) has recently been put in use at NVSL.

To enhance its ability to trace animals, the USDA has assigned top priority to implementation of a verifiable system of national animal identification. Development of this system in cattle has been underway for over a year and a half. Under the auspices of APHIS, a partnership of industry, State, and Federal officials was formed in 2002 to uniformly coordinate the national animal identification plan. A draft plan was presented at the annual U.S. Animal Health Association meeting in October 2003. This draft plan would provide for implementation in three phases: (1) premises identification, (2) individual or group/lot identification for interstate and intrastate commerce, and (3) retrofitting remaining processing plants, markets, and other industry segments with appropriate technology to enhance tracking of animals throughout the marketing and

slaughter chain. Further details of the draft plan are available on the U.S. Animal Identification Plan Web site at http://www.usaip.info/.

USDA continues to expand its educational activities. It has developed and distributed extensive educational and training materials in the past, and new materials are being developed to reflect the recent regulatory changes. USDA has collaborated extensively with academic, professional, trade and consumer organizations in this effort.

In addition, since BSE became a reportable disease in the United States in 1986, USDA has conducted an active and effective Awareness Program on BSE for veterinarians, farmers, and other personnel involved in the transportation, marketing, and slaughter of cattle for more than a decade. Specifically, in May 1990, USDA began educational outreach to veterinarians, cattle producers, and laboratory diagnosticians regarding the clinical signs and diagnosis of BSE. These activities have been broadened both in terms or scope and targeted audiences in recent years, and USDA continues to educate U.S. cattle producers, veterinarians, industry groups, and the general public on BSE through frequent briefings and press conferences. In addition to press releases and fact sheets, a videotape on BSE and an information packet have been distributed to all APHIS field offices, State veterinarians, extension veterinarians, colleges of veterinary medicine, and industry groups. USDA also maintains an extensive BSE Web site at http://www.aphis.usda.gov/.

The actions taken before December 30, 2003, and the actions taken since diagnosis of BSE in Washington State demonstrate that, although rigorous measures were already in place to safeguard human and animal health in the United States, the United States is continually working to improve its national program. APHIS concludes that the additional measures in place since the original risk analysis further limit the potential for exposure of animals or humans in the United States to BSE.

Actions being taken in Canada

CFIA reported that the latest finding of a BSE-infected cow with BSE did not change its assessment of the situation in North America with respect to the safety of the food supply. The finding of a small number of additional cases has never been excluded and is consistent with the report of the International Panel of BSE experts who reviewed and commended Canada's program.

However, in response to the detection of the infected animal of Canadian origin in Washington State, CFIA initiated an epidemiological investigation. This investigation was concurrent and cooperative with the United States investigation of animals from the same herd of origin. CFIA initially identified 12 animals of interest from the herd and is considering additional tracing efforts. In addition, CFIA continues an extensive epidemiological investigation into the feed sources of the herd of origin.

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As part of its on-going policy considerations, CFIA made enhancements to the measures that it had strengthened in response to the diagnosis of the BSE-infected animal in Canada. Relevant to this, CFIA plans to test a minimum of 8,000 animals over the next 12 months, and will continue to increase that number progressively. The ultimate number of animals tested will reflect international standards existing at the time. These are expected to be revised over the next one to two years.

Testing will focus on those animals most at risk for BSE. These include animals demonstrating clinical signs consistent with BSE, so-called downer animals (those unable to stand or move without assistance), as well as animals that have died on the farm, are diseased, or must be destroyed because of serious illness. A sample of healthy older animals will also be tested. Provincial government officials will play a significant role in the surveillance activities.

As in the United States, an international team of animal and human health experts reviewed the situation in Canada. A summary report is posted on the CFIA Web site at http://www.inspection.gc.ca/english/anima/heasan/disemala/bseesb/evalsume.shtml. Enhancements recommended by the international team of experts are being introduced to strengthen Canada's cattle identification program. The identification program provided invaluable information about the BSE-infected cow's background during the investigation last May. Enforcement of the program will be increased, as will research into new technologies to detect disease. CFIA will also foster linkages and integration with provinces, territories, industry and trading partners, to expand its resources. Health Canada (the agency responsible for human health in Canada) is also enhancing its capacity to identify and trace the presence of bovine-derived material in the products it regulates.

The Canadian Government has worked in close consultation with provincial, territorial, industry and U.S. representatives during the development of these measures. This collaboration will continue in order to ensure that enhancements are effectively and efficiently implemented.

Furthermore, CFIA has taken actions in response to United States policy changes. After the United States prohibited the slaughter of non-ambulatory animals for human consumption, it imposed a similar requirement on countries that export meat to the United States. In response to this requirement, on January 13, 2004, CFIA announced that all downers are banned from slaughter in Canadian registered establishments eligible for export to the United States.

For additional information, see the news release dated January 9, 2004, located at the CFIA Web site: http://www.inspection.gc.ca/.

Exposure assessment conclusions

In the original analysis of Canada, APHIS' Veterinary Services (VS) considered the sum total of the control mechanisms (e.g., effectiveness of surveillance, import controls, and feed ban) in place at the time of the diagnosis and the actions taken after it (e.g., epidemiological investigations, depopulation) to be adequate, as long as the mitigations described in the analysis and the proposed rule were applied. APHIS' analysis indicated that the mitigations should be effective in addressing the risk of importing BSE from Canada. However, not only have we made the enhancements described above to our own system, but also we are in regular contact with Canadian officials about BSE policy development in Canada. U.S. policy changes, such as removal of SRMs from human food and increased surveillance, are in accord with similar approaches being taken in Canada.

We are holding ongoing discussions in anticipation of developing a North American strategy.

However, even without the institution of the additional measures, the animal would not have been imported into the United States under the conditions of the proposed rule. Therefore, the conclusions of the original exposure assessment remain unchanged. In summary, the fact that only two indigenous cases of BSE have been identified as Canadian in origin, the existence of strong BSE controls in Canada, and the importation restrictions VS would impose before allowing these imports make it unlikely that BSE would be introduced from Canada under the conditions described in the proposed rule. With regard to assessing exposure, the Harvard study suggested that the measures taken by the U.S. Government and industry give the United States an effective program to preclude the spread of BSE to animals should it be introduced into this country. These measures, which have been enhanced significantly since the original analysis, will further ensure that these risks remain low.

Consequence assessment

As a practical matter, the diagnosis of BSE in the cow had significant consequences in the United States in terms of human and financial resources and lost trade in ruminants and ruminant products. However, the infected animal would not have been imported under the conditions assessed in the analysis and defined in the proposed rule. Therefore, VS maintains that the consequences with regard to animal health, human health, and the environment continue to be minimal or low under the conditions described in the risk analysis and proposed rule.

Risk Estimate

In summary, we reiterate the conclusion reached in the original risk estimate. Under the conditions described in the analysis and proposed rule, VS considered the risk of BSE infected animals or animal products entering the United States from Canada

under the conditions described in the analysis and proposed rule and exposing US livestock through feeding of infected materials to susceptible animals to be low.

Comment

As noted above, the USDA has responded to the detection of the case of BSE in an imported BSE-infected cow with significant BSE risk mitigation measures in this country. Perhaps most importantly, parts of slaughtered animals that are considered at particular risk of containing the BSE agent in an infected animal (SRMs) have been banned from the human food supply. Specifically, FSIS has established the skull, brain, trigeminal ganglia, eyes, vertebral column, spinal cord, and dorsal root ganglia of cattle over 30 months of age, as well as the tonsils and small intestine of cattle of all ages, as SRMs. Furthermore, FSIS prohibits such SRMs from the human food supply. The Canadian Government established similar safeguards in Canada.

The measures taken by FSIS do not restrict the slaughter of cattle in the United States based on the age of the animals. In this regard, meat from cattle 30 months of age or older will continue to be allowed into the human food supply. However, measures are in place to ensure that SRMs from such cattle do not enter the food supply. We now believe it would not be necessary to require that beef imported from BSE minimal-risk regions be derived only from cattle less than 30 months of age, provided equivalent measures are in place to ensure that SRMs are removed when the animals are slaughtered and that such other measures as necessary are in place. We believe such measures are already being taken in Canada.

Enclosure

A Case of Bovine Spongiform Encephalopathy (BSE) in the United States
As of February 4, 2004

Executive Summary

On December 23, 2003, the U.S. Department of Agriculture (USDA) announced a presumptive positive case of BSE in a Holstein cow slaughtered in the State of Washington. The infected cow entered the United States on September 4, 2001, as part of a shipment of 81 animals from the source herd in Canada. Of these 81 animals, 25 were considered to be higher risk as defined by the Office International des Epizooties (OIE): animals born on a known source premises within 12 months of an affected animal, either before or after.

Counting the index animal, USDA has definitively accounted for 14 of the 25 animals considered to be higher risk. In total, USDA has accounted for 29 of the 81 cattle in the initial shipment, plus 7 additional animals also dispersed from the birth herd. The number of animals found is consistent with the number expected after analysis of regional culling rates. The epidemiological investigation is currently yielding little additional information. USDA is therefore concluding active investigation and culling activities at this time.

A total of 255 cattle have been depopulated from 10 premises on which one or more source herd animals were found. This number includes the 35 animals definitively identified as originating from the source herd (aside from the index cow), as well as any other cattle on those 10 premises that could possibly be from the Canadian source herd. Out of an abundance of caution, all 255 animals were depopulated and tested for BSE; all of the animals tested negative. Because there is a small probability that BSE can be transmitted maternally, the two live offspring of the infected cow were also euthanized. A third had died at birth in October 2001. All carcasses were properly disposed of in accordance with Federal, State, and local regulations.

Emergence of a Single Case of BSE

The index cow had difficulty giving birth to a bull calf on November 29, 2003, and was subsequently sent to slaughter. On December 9, 2003, the animal was observed to be nonambulatory (a “downer” animal). Accordingly, as part of USDA’s targeted BSE surveillance program, brain samples were taken from the animal and sent to USDA’s National Veterinary Services Laboratories (NVSL) in Ames, Iowa, for testing. After NVSL’s presumptive positive finding, samples were hand-carried to the OIE reference laboratory in Weybridge, England, for final confirmatory testing according to international animal health requirements. On the morning of December 25, 2003, the OIE reference laboratory confirmed USDA’s diagnosis of BSE.

Even before the confirmation from Weybridge, the presumptive positive result at NVSL triggered an epidemiological investigation by Federal and State officials. Immediately, USDA's Animal and Plant Health Inspection Service (APHIS) activated its Emergency Operations Center (EOC) in Riverdale, Maryland; and representatives from APHIS' Transmissible Spongiform Encephalopathy Working Group as well as emergency response leaders were mobilized to begin an aggressive investigation.

The positive cow was traced from the slaughter plant back to a 4,000 cow dairy herd near Mabton, Washington. This herd (the index premises) was placed under quarantine on December 23, 2003, to prevent further complications to traceback and traceforward investigations. In Washington State, USDA and State officials mobilized an Area Command office in Olympia and an Incident Command Post in Yakima. Both offices worked in close contact with the APHIS National Coordinating Group at the EOC.

Investigative Details Regarding the BSE-Positive Cow

The cow, known to be approximately 6 years and 8 months old at slaughter, was purchased into the Mabton herd in October 2001. The cow was culled from the herd due to paralysis resulting from calving complications. She had given birth to two live offspring in the United States. A bull calf born November 29, 2003, was sold to a calf-raising facility in Sunnyside, Washington, and the other calf, a yearling heifer, was known to be present in the Mabton herd.

Tracing Back the BSE-Positive Cow

On January 6, 2003, Dr. Ron DeHaven, USDA's Chief Veterinary Officer, and Dr. Brian Evans, Canada's Chief Veterinary Officer, held a joint press conference to announce that DNA evidence indicated—with a high degree of certainty—that the BSE-positive cow found in Washington State originated from a dairy farm in Calmar, Alberta, Canada. The DNA evidence is based on comparative testing of DNA from the brain of the positive cow with DNA from semen of her sire and with blood from the heifer calf born from the BSE-positive cow on the index farm. The test results were independently confirmed by both U.S. and Canadian animal health laboratories. Breeding records for the heifer calf confirmed that the animal was born from the cow bearing the tag number found on the BSE-positive cow at slaughter and found in the records on the farm in Alberta. This DNA information, coupled with information obtained from the owner of the index farm in Mabton, Canadian officials, and import records, adds certainty to the accuracy of the traceback to Alberta.

Other elements of this investigation continued in both the United States and Canada and provided additional information. U.S and Canadian officials are actively communicating as they continue a feed investigation. While it is clear that the BSE-positive cow originated in Canada, U.S. and Canadian officials are cooperating fully to address the issue.

Details Regarding Cohorts

On December 31, 2003, USDA determined that a Canadian health certificate, signed on August 30, 2001, listed 82 eartag numbers from cattle that were part of the source herd dispersal in Calmar, Alberta, Canada. One of those eartag numbers matched the number on the BSE-positive cow. It has been confirmed that 81 of those 82 animals crossed the border into the United States on September 4, 2001, through the port of Oroville, Washington. Of these 81 animals, 25 were considered to be higher risk as defined by the OIE: animals born on a known source premises within 12 months of an affected animal, either before or after.

Through February 4, 2004, task force members performed 185 herd investigations, including 52 complete herd inventories totaling over 75,000 cattle, in an effort to find any cattle that may have entered the United States from the source herd in Alberta. Counting the index animal, USDA has now definitively accounted for 14 of the 25 animals considered to be higher risk. In total, USDA has accounted for 29 of the 81 cattle that entered on September 4, 2001: 1 was the index cow from Mabton; 9 were on the index premises near Mabton; 3 were located on a nearby premises in Mattawa, Washington; 1 was on a premises in Quincy, Washington; 3 were on a dairy in Tenino, Washington; 6 were on a dairy in Connell, Washington; 1 was on a dairy in Moxee, Washington; 1 was on a dairy in Othello, Washington; 3 were on a dairy in Burley, Idaho; and 1 was on a second dairy (not the index premises) in Mabton, Washington.

In addition to those 81 cattle, another 17 heifers were sold at the source herd dispersal in Calmar, Alberta. Although the total number of those 17 that entered the United States is not known, 7 have now been located: 3 were on a dairy in Quincy, Washington; 1 was on a dairy in Boardman, Oregon; 1 was on a dairy in Othello, Washington; 1 was on a dairy in Burley, Idaho; and 1 was on a second dairy (not the index premises) in Mabton, Washington. The animal on the second Mabton premises was actually an earlier offspring of the index cow born in December 2000 in Alberta. A chart diagramming the source herd animal movements can be found at the end of this document.

A total of 255 cattle have been depopulated from 10 premises where 1 or more source herd animals were found. This total includes the 35 animals definitively identified as originating from the source herd (aside from the index cow), as well as any other cattle on those 10 premises that could possibly be from the Canadian source herd. None of the 255 cattle tested positive for BSE. The carcasses of the euthanized animals were held until the test results were returned; after receiving the negative results, the carcasses were disposed of in a landfill in accordance with all Federal, State, and local regulations.

Actions Taken on the U.S. Offspring of the BSE-Positive Cow

After it was determined that the bull calf delivered by the positive cow in late November 2003 was sold to a calf-raising facility in Sunnyside, Washington, State officials immediately quarantined that premises. Identification of animals was incomplete, so

APHIS determined that, out of an abundance of caution, all animals on the premises should be euthanized. On January 6, 2004, APHIS personnel gathered the animals from the Sunnyside premises and transferred them to a slaughter facility in Wilbur, Washington. All 449 animals were humanely euthanized. The remains of those animals were delivered to a landfill on January 8, 2004. The yearling heifer in the Mabton herd that was definitively identified to be the offspring of the BSE-positive cow, along with 130 other cattle from the Mabton herd with known or potential risk for having been infected with the BSE agent in Canada, have been euthanized.

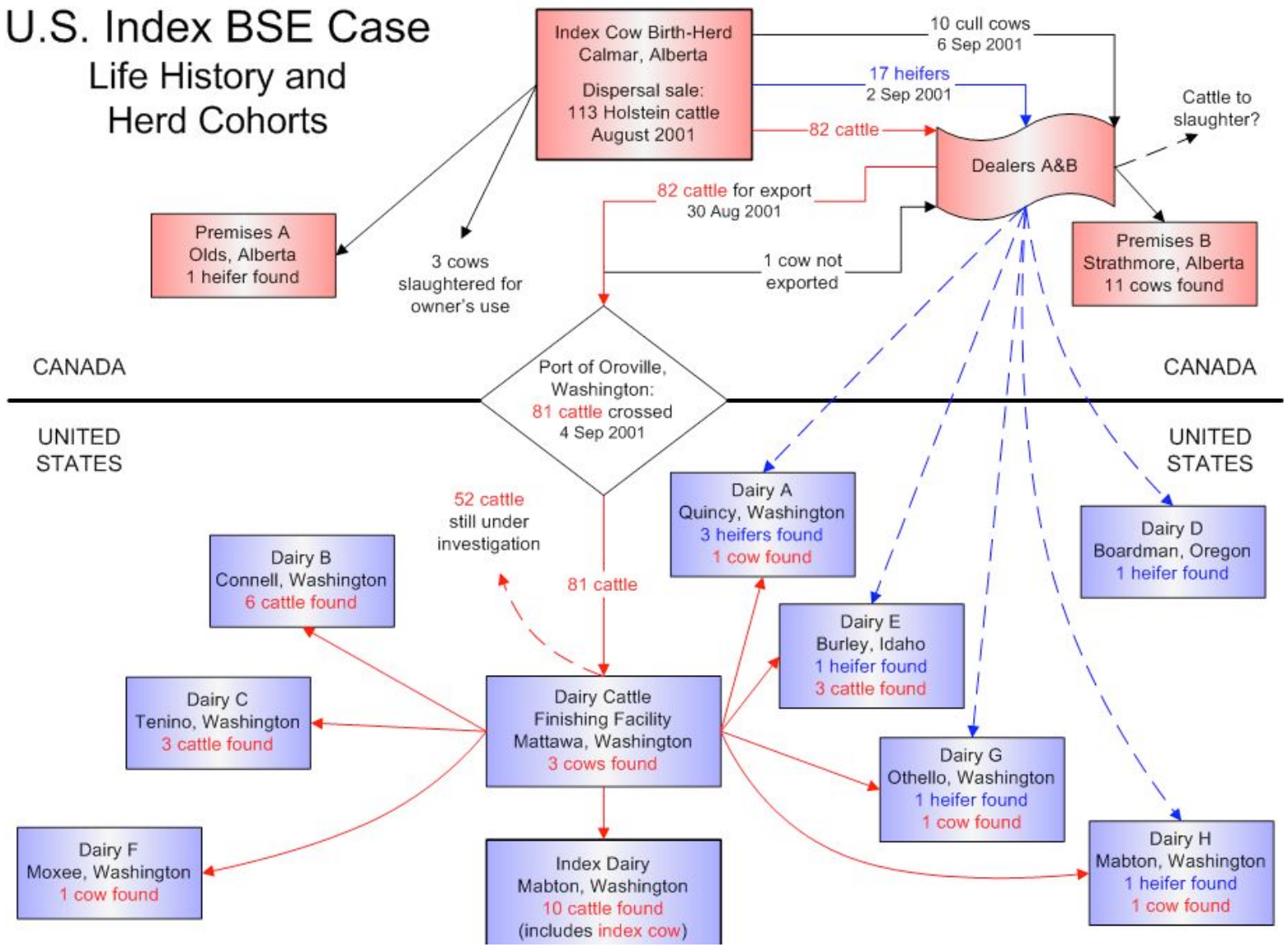
Collaboration with the Food and Drug Administration (FDA) Feed Investigation

On December 27, 2003, FDA announced that its investigators and inspectors from the States of Washington and Oregon had located all potentially infectious product rendered from the BSE-positive cow in Washington. The rendering plants that processed all the nonedible material from the BSE cow have placed a voluntary hold on all potentially infectious products. The rendering firms, located in Washington and Oregon, have assisted and cooperated fully with FDA's investigation. This product is being disposed of in a landfill in accordance with Federal, State, and local regulations. FDA also reported that the feeding and feed mixing practices related to the Mabton index premises were in full compliance with all mammalian protein restrictions and other regulations.

Conclusion

This investigation demonstrates that the affected animal was not indigenous (not born in the United States) and that her exposure to the causative agent of BSE occurred in Canada. As provided in the OIE Code (Article 2.3.13.4), her progeny born in the previous 2 years (the heifer calf in 2002 and bull calf in 2003) were identified and destroyed.

Appendix 2: Explanatory Note: Risk Analysis: BSE Risk from Importation of Designated Ruminants and Ruminant Products from Canada into the United States; Animal and Plant Health Inspection Service, Veterinary Services, February 2004



Appendix 3: Cohen, J. and G.M. Gray, Harvard Center for Risk Analysis, Response to Comments Submitted in Response to USDA's Proposed Rule on Importing Beef and Beef Products from Canada. Memorandum submitted to USDA on June 18, 2004.

Appendix 3: Cohen, J. and G.M. Gray, Harvard Center for Risk Analysis, Response to Comments Submitted in Response to USDA's Proposed Rule on Importing Beef and Beef Products from Canada. Memorandum submitted to USDA on June 18, 2004.

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Appendix 3: Cohen, J. and G.M. Gray, Harvard Center for Risk Analysis, Response to Comments Submitted in Response to USDA's Proposed Rule on Importing Beef and Beef Products from Canada. Memorandum submitted to USDA on June 18, 2004.

Summary

We have addressed comments raised by Dr. Louis Anthony Cox, working on behalf of the Ranchers-Cattleman Action Legal Fund (RCALF), on the use of the Harvard Center for Risk Analysis (HCRA) BSE Analysis to support a USDA proposed rule on trade in cattle and cattle products with Canada. Specifically, we address the role of the "worst case" analysis in the Harvard BSE Report along with some specific comments related to assumptions or the interpretation of predictions made by the Harvard BSE model.

Dr. Cox's comments focus on HCRA's original finding (Cohen 2001; Cohen 2003) that assigning "worst case" values to certain parameters can lead to the prediction that the infection reproductive constant (R_0) will exceed 1.0. An R_0 greater than 1.0 implies that the disease can spread and the prevalence will grow if it is introduced into the U.S. herd. To address this issue we have first updated the "worst case" assumptions for parameters for which new and better data have become available, and second we use the Harvard BSE model to explore the extent to which our estimate of R_0 depends on assumptions regarding the misfeed rate, they key parameter for which we could identify no new information.

We update the Harvard model with new data from the Food and Drug Administration (FDA) addressing two critical model parameters – mislabeling of products containing prohibited ruminant protein and contamination of nonprohibited products with prohibited protein. There are no data to further address a third important parameter, the rate at which prohibited material is deliberately fed to cattle ("misfeeding"). We use the Harvard BSE model to identify the rate of misfeeding necessary to result in a substantial probability that R_0 will exceed 1.0. We also examine the distribution of predicted values for R_0 when it does exceed 1.0.

Because the value of R_0 determines whether the number of cattle with BSE tends to grow or decrease over time, its value is critical to the determination of potential human exposure to BSE and the impact of BSE on animal health. Values close to 1.0 imply that the disease will either spread slowly (R_0 slightly more than 1.0) or slowly die out (R_0 slightly less than 1.0). Values of R_0 substantially greater than 1.0 imply that the disease will spread rapidly, while values substantially less than 1.0 imply that it will die out relatively rapidly. Our analysis suggests that if less than 7.5% of prohibited feed is given directly to cattle (*i.e.*, less than about 1 in 13

batches), then we can be confident that R_0 is less than 1.0. The expected value of R_0 is less than 1.0 even when we assume the misfeed rate is as high as 15%. Even under those circumstances when the Harvard model predicts $R_0 > 1.0$, the amount by which R_0 exceeds this threshold is limited, implying that the disease would spread slowly (assuming no further mitigation measures are taken). Data to characterize the misfeed rate would be very useful to further address this issue. It may be possible to judge whether a misfeed rate of more than 7.5% is even plausible with a relatively small amount of investigation.

We respond to Dr. Cox's comments about potential sources of uncertainty. In some cases, these sources of uncertainty have been addressed in Harvard's earlier analyses. Although other sources of uncertainty have not been explicitly addressed in either Harvard's earlier analyses or in USDA's risk assessment, we explain why we do not believe they undermine USDA's conclusions. In other cases, where the sources of uncertainty are speculative, we note that the R-CALF comments do not provide sufficient scientific reasoning or data to evaluate the plausibility of the underlying claim. If further information could be developed, some of the proposed sources of uncertainty may be addressed. Finally, we do not address those comments that do not pertain to the Harvard BSE model, or to how it has been used by USDA.

Introduction

In October, 2003, USDA published an analysis evaluating the impact of importing ruminants and ruminant products from Canada into the U.S. (U.S. Department of Agriculture 2003). The analysis was conducted as part of the rulemaking procedure for a proposed easing of the ban on importation of bovines from Canada that was imposed following the discovery of an indigenous BSE case in that country in May, 2003. The proposed rules would allow the import of cattle under the age of 30 months and certain ruminant products from Canada.

In public comments submitted to the Department, Dr. Louis Anthony Cox, on behalf of the Ranchers-Cattleman Action Legal Fund (RCALF) criticized that assessment on several grounds (Cox 2004). This memo addresses two sets of issues raised by Dr. Cox. First, Dr. Cox notes that USDA's assessment proceeded on the assumption that the "base case" described in

Harvard's BSE risk assessment[2] is valid. Although the base case assumptions identified by Harvard suggest that BSE would not spread widely upon introduction into the U.S., the worst case assumptions in that assessment suggest that it could. Second, Dr. Cox suggests that USDA did not consider several important sources of uncertainty (see list on pp. 12-13 of (Cox 2004)). This memo addresses these points.

1 Evaluation of the Worst Case Scenario

1.1 Background

The Cox comments point out that if a series of worst case assumptions identified by Harvard are assumed to be true, then the BSE reproductive constant, referred to as "R_0" might exceed unity. This condition implies that each infected animal infects more than one animal on average, leading to growth over time in the number of cattle with BSE. The opposite condition, *i.e.*, $R_0 < 1$, implies that the number of cattle with BSE decreases over time. Because R_0 determines whether the number of cattle with BSE grows or decreases over time, its value is critical to the determination of potential human exposure to BSE and the impact on BSE on animal health.

The value of R_0 depends, in turn, on the values assigned to numerous parameters in the Harvard BSE simulation model. However, as explained in Section 4.2.1 of Harvard's 2003 report (see Figures 4-1 and 4-2), most parameters have only a limited influence on the value of R_0, meaning that even when they are assigned their "worst case" values, the value of R_0 does not change substantially from what is predicted when all the parameters are assigned their "base case" values. The "base case" values represent our best estimate of what is likely to be representative of conditions in the U.S.

When we assigned worst case values to some of the model parameters individually while assigning base case values to all of the other parameters, the Harvard simulation model predicted a substantially larger number of infected cattle following the introduction of BSE into the U.S., thus suggesting a substantially higher R_0 value. As illustrated in Figure 4-1 of Cohen *et al.*

[2] Cohen, J.T., Duggar, K., Gray, G.M., and Kreindel, S. 2003. Evaluation of the Potential for Bovine Spongiform Encephalopathy in the United States. Available at http://www.hcra.harvard.edu/pdf/madcow.pdf. October.

(2003), the parameters having the most important impact on R_0 included: 1) the misfeeding rate (proportion of correctly labeled prohibited feed that is incorrectly administered to cattle); 2) the feed mislabeling rate (proportion of prohibited feed incorrectly labeled as non-prohibited)[3]; and 3) the render reduction factor (amount by which rendering treatment reduces the amount of BSE infectivity).

Assigning worst case values simultaneously to multiple parameters lead to even greater deviations from the base case predictions (see Figures 4-2 and 4-4 in Cohen *et al.* (2003)). Although such a scenario seems unlikely, the Harvard assessment did not quantify the relative plausibility of the base case and the worst case parameter values. As Cox (2004) notes (p. 9), "... *the probabilities of 'worst-case' assumptions sufficient to cause spread (over at least some area) have not been assessed in either the USDA Risk Analysis or the Harvard Study.*" It is for this reason that the Harvard study recommended further research to better characterize these assumptions (see lines 3820-3838 in that report).

When Harvard conducted its original analysis in 2001 (Cohen 2001), establishing realistic bounds on some of the critical parameters was complicated by the limited amount of available information. We judged government feed ban compliance surveillance data to be inadequate for risk assessment purposes for two reasons. First, the surveillance data indicated the fraction of facilities out of compliance with feed ban regulations, rather than the fraction of all prohibited material passing through non-complying facilities. Second, the surveillance data did not differentiate between technical (*e.g.*, incorrect paperwork) violations of the regulation and substantive violations. Because we chose not to rely on this surveillance data, we instead had to estimate the frequency of violations indirectly. Section 2.16.4 of Appendix 1 in Cohen *et al.* (2003) describes our use of a mass balance approach to estimate mislabeling, contamination, and misfeeding probabilities.

[3] There is a typographical error in Figures 4-1 and 4-3 of Cohen *et al.* Cohen, J. T., Duggar, K., Gray, G. M. and Kreindel, S. (2003). *Evaluation of the Potential for Bovine Spongiform Encephalopathy in the United States: Report to the U.S. Department of Agriculture (revised October, 2003)*. Boston, MA, Harvard Center for Risk Analysis. Available at: http://www.hcra.harvard.edu/pdf/madcow.pdf.. The second to last item on the horizontal axis ("3.2.3.5 Render Mislabel") should read "3.2.3.5 Render Mislabel".

1.2 Methodology

We use the Harvard BSE simulation (Cohen 2003) to estimate the magnitude of R_0. We approximate this parameter as the ratio of the number of animals infected due to transmission from other U.S. cattle to the number of U.S. cattle potentially causing infection over a 20-year simulation period following the introduction of 1,000 cattle oral ID_{50}s into the feed supply. The numerator of this ratio (number of animals infected due to transmission from other U.S. cattle) includes animals infected due to 1) consumption of contaminated feed (not including the feed introduced at the beginning of the simulation), 2) consumption of contaminated blood meal, or 3) maternal transmission. The denominator of the R_0 ratio includes BSE-infected animals that died during the simulation because it is those animals that contribute to contamination of feed and blood meal.

Our estimate or R_0 omits from the denominator cattle contributing to maternal transmission that do not die during the simulation. This inflates our estimate of R_0 (because it decreases the denominator), but the distortion is likely to be small. First, the number of maternal transmission cases is a small fraction of total cases (30 out of 220 infected following the import of 500 cattle – see Section 3.2 Appendix 3A in Cohen *et al.* (2003)). Second, the omission occurs only if the cow transmitting disease does not die during the 20-year simulation.

Each simulation trial (*i.e.*, each 20-year simulation run) produces an estimate of R_0. The R_0 values calculated for each of multiple simulation trials results collectively represent a distribution for the R_0 parameter. We develop distributions for R_0 that correspond to the assignment of worst case values to all of the parameters characterizing MBM production, feed production, and feed administration. Table 3-9 in Cohen *et al.* (2003) details these values. For this analysis, we use the same values with the exception of the mislabeling rate and the misfeeding rate.

1.2.1 Mislabeling and Contamination

This report uses the most recent government surveillance data to estimate probabilities for mislabeling and contamination in MBM and feed production facilities. Mislabeling occurs when a producer incorrectly labels prohibited product as non-prohibited. Contamination occurs when a prohibited product crosses over into non-prohibited product. Contamination can occur in

mixed facilities (facilities that produce both prohibited and non-prohibited product on the same line) and is presumably made worse by incomplete cleanout procedures when production is switched from prohibited to non-prohibited product.

Since the publication of Harvard's November, 2001 BSE risk assessment (Cohen 2001), additional information on compliance with the 1997 feed rule has become available. The United States Food and Drug Administration Center for Veterinary Medicine (CVM) has collected and disseminated the state and U.S. FDA inspection results for facilities that handle prohibited material (i.e., ruminant derived protein, with some exceptions). This information[4] quantifies the number of facilities out of compliance with the feed rule and hence serves as a useful starting point for our analysis. However, because the U.S. FDA databases do not report the size of these facilities (*i.e.*, total material throughput), we have to make an assumption regarding the relative size of the non-compliant facilities relative to other facilities. For this purpose, we conservatively estimate that the non-compliant facilities are the same size on average as facilities not cited for feed rule violations. This assumption is likely to be conservative because it has been the observation of inspectors that smaller firms are more likely to be cited for violations than larger ones (Personal communication, Neal Bataller, FDA/CVM, May, 2004).

In order to estimate mislabeling and contamination probabilities, we rely on data collected by FDA/CVM[5] prior to September, 2003. Use of data collected prior to the December 23, 2003 discovery of a BSE case in Washington state is probably conservative because compliance rates have most likely improved in the wake of that discovery. In any case, FDA/CVM data collected prior to September, 2003 better detail the nature of the violations discovered, reporting the total number of firms with at least one violation and designating each violation as a case in which: 1) products were not labeled as required, 2) the facility did not have adequate systems to prevent co-mingling, or 3) the facility did not adequately follow record keeping regulations. More recent data report violations only in terms of the type of action indicated – i.e., Official Action Indicated (OAI), Voluntary Action Indicated (VAI), or No Action Indicated (NAI). FDA (U.S. Food and Drug Administration 2003) defines these terms[6].

[4] (http://www.fda.gov/cvm/index/bse/bse_updates.htm) and the online database of current inspection status (http://www.accessdata3.fda.gov/BSEInspect)

[5] Compliance program implementation details can be found at http://www.fda.gov/cvm/index/cpg/7371-009.doc.

[6] According to FDA, "An OAI inspection classification occurs when significant objectionable conditions or practices were found and regulatory sanctions are warranted in order to address the establishment's lack of

Table 1 reproduces the April 2002 FDA Update (U.S. Food and Drug Administration 2002), the most recent summary reported prior to the September, 2003 change in database and reporting details. The data summarized here are limited to facilities handling prohibited materials.

Table 1
April, 2002 Results of Inspections at Facilities Handling Prohibited Materials

Facility Type	Inspected (N)	Cited for Mislabeling (N)	Cited for Mislabeling Percent	Cited for Comingling (N)	Cited for Comingling Percent
Renderers	171	4	**2.3%**	3	**1.8%**
Feed mills					
Licensed Feed Mills	370	8	2.2%	2	0.5%
NL Feed Mills	1224	55	4.5%	28	2.3%
Total	1594	63	**4.0%**	30	**1.9%**
Other Firms(a)	2153	77	3.6%	34	1.6%

Notes:

(a) Other firms include ruminant feeders, on-farm mixers, protein blenders, and distributors

The parameters adopted for our analysis are highlighted in Table 1 and reproduced in Table 1 for the purpose of comparing them with assumptions made in our earlier risk assessment (Cohen 2003).

compliance with the regulation. An example of an OAI inspection classification would be findings of manufacturing procedures insufficient to ensure that ruminant feed is not contaminated with prohibited material. Inspections classified with OAI violations will be promptly re-inspected following the regulatory sanctions to determine whether adequate corrective actions have been implemented."

"A VAI inspection classification occurs when objectionable conditions or practices were found that do not meet the threshold of regulatory significance, but do warrant advisory actions to inform the establishment of findings that should be voluntarily corrected. Inspections classified with VAI violations are more technical violations of the Ruminant Feed Ban provisions such as minor recordkeeping lapses and conditions involving non-ruminant feeds." U.S. Food and Drug Administration (2003). *Update on Ruminant Feed (BSE) Enforcement Activities (September 30, 2003)*. Center for Veterinary Medicine. Available at: http://www.fda.gov/cvm/index/updates/BSEInspec03.htm..

Table 2
Assumptions for Mislabeling and Contamination

Parameter	MBM Production			Feed Production		
	Base Case (2003)[(a)]	Worst Case (2003)[(a)]	Revised Worst Case[(b)]	Base Case (2003)[(a)]	Worst Case (2003)[(a)]	Revised Worst Case[(b)]
Probability of Contamination	14%	25%	1.8%	16%	16%	1.9%
Proportion of Prohibited Material Transferred to Non-Prohibited Material per Contamination Event	0.1%	1%	1%	0.1%	1%	1%
Mislabeling Probability	5%	10%	2.3%	5%	33%	4%

Notes:

(a) Values from Cohen et al. (2003).
(b) Values developed for this assessment.

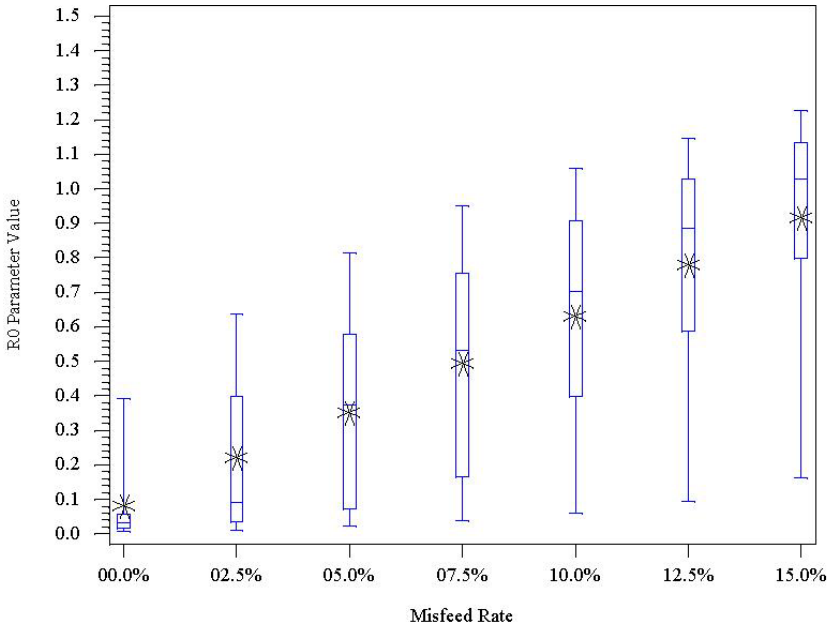
1.2.2 Misfeeding

We do not have new information on the value of the misfeeding parameter and therefore continue to assume that it could be as great as 15%. However, because this parameter has the greatest influence on the predicted number of infected cattle following the introduction of BSE into the U.S., we ran multiple sets of simulations to determine how its value influenced the predicted R_0 distribution. Values tested included 0%, 2.5%, 5%, 7.5%, 10%, 12.5%, and 15%.

1.3 Results

Figure 1 illustrates the distribution of the R_0 parameter as a function of the assumed misfeeding rate. Each box and whiskers plot identifies the distribution median (horizontal line through the middle of the box), the first and third quartiles (extreme ends of the box), and the 5th and 95th percentiles (extreme ends of the "whiskers"). The asterisk designates the distribution mean. Each distribution is based on the results of 5,000 simulation trials. Appendix A details the summary statistics for these distributions along with the confidence intervals on those statistics.

Figure 1
Distribution of R_0 Values as a Function of the Assumed Misfeeding Rate



The results show that the 95th percentile value for R_0 remains less than unity so long as the misfeeding rate is no more than 7.5%. Even when higher misfeeding rates are assumed, the value of R_0 does not substantially exceed unity. If we assume a misfeeding rate of 15%, the 95th percentile value for R_0 is 1.23. Under these conditions, it would take more than three incubation cycles on average for the number of BSE-infected animals in the U.S. to double following the introduction of the disease.

2 Addressing other sources of uncertainty identified by Dr. Cox

Dr. Cox identifies sources of uncertainty that he states USDA should address in the Department's risk assessment (see bullet list on pp. 12-13 in (Cox 2004)). We comment on each of these below.

2.1 The roles of horizontal and vertical transmission (if any)

Despite the absence of direct evidence for maternal transmission of BSE, the Harvard simulation base case assumes that such transmission is possible. In particular, we assume that

during after 5/6 of the incubation period has elapsed, disease will be transmitted from cow to calf with 10% probability. These assumptions have been made in the analysis described in this memo.

In the base case analysis described by Harvard in its October, 2003 report (Cohen 2003), 15% of the BSE transmissions were attributable to maternal transmission (see Section 3.2.1.5 in that report). This relatively small proportion suggests that if it does occur, maternal transmission is a relatively unimportant mode of transmission.

2.2 Susceptibility distribution within cattle of the same age

The possibility that susceptibility differs among cattle of the same age does not substantively influence the spread of disease predicted by the Harvard simulation model. The Harvard simulation model estimates the probability of disease transmission as the product of susceptibility and exposure. In particular, the probability of infection is estimated to be one-half the number of oral ID_{50}s in consumed feed, scaled by a "susceptibility factor" that is a function of age. There is no evidence that susceptibility differs substantially among animals of the same age. Nonetheless, even if it did, the result would be that our model would underestimate the risk of infection for some animals but overestimate for others. For any scenario involving more than a small number of BSE-exposed cattle, the average actual susceptibility would not differ substantially from the estimated value used by the model. Therefore, even if susceptibility does vary among animals of the same age, there is no reason to believe that the Harvard model would substantially underestimate (or overestimate) the degree to which the disease would spread among cattle or the degree to which humans would be exposed to BSE-contaminated food.

2.3 Variability on virulence of different new BSE cases

Dr. Cox does not present any evidence that virulence differs substantially from one BSE case to another. Nor does he explain why differences in virulence would affect the critical outcomes of a risk assessment, namely the total number of cattle that become infected and total human exposure to BSE.

2.4 Proportion of infected animals in Canada

This issue does not bear directly on USDA's use of the Harvard simulation model in the Department's risk assessment.

2.5 The detection probability per case (and hence the number of true cases per observed case)

This issue does not bear directly on USDA's use of the Harvard simulation model in the Department's risk assessment.

2.6 The age distribution at first infection

This issue does not bear directly on USDA's use of the Harvard simulation model in the Department's risk assessment.

2.7 The latency period (and its distribution) until expression

The Harvard simulation model assumes that the latency period (*i.e.*, the duration between exposure and manifestation of disease signs) can vary among exposed animals. For example, we assume in the base case that this latency period is no more than 26 months with 1% probability. The specific distribution used is based on the statistical analysis of the BSE epidemic in the UK conducted by Fergusson *et al.* (1997).

2.8 The potential for clustering of rare events within geographic areas, processing plants, affected populations, *etc*.

This possibility is presumably of potential importance because it raises the possibility of a "mini-epidemic" starting in a region of the U.S. that effectively acts as a closed system with unfavorable characteristics (*e.g.*, rendering facilities that use technologies with limited ability to reduce infectivity). However, Dr. Cox does not present any evidence or data to identify such a region if it does exist.

Appendix 3: Cohen, J. and G.M. Gray, Harvard Center for Risk Analysis, Response to Comments Submitted in Response to USDA's Proposed Rule on Importing Beef and Beef Products from Canada. Memorandum submitted to USDA on June 18, 2004.

2.9 The status and extent of current and future compliance and attendant consequences of non-compliance (such as mislabeling, *etc*.) in Canada and the U.S.

This issue does not bear directly on USDA's use of the Harvard simulation model in the Department's risk assessment.

2.10 Possible heterogeneity of R_0 in different geographic areas or for different strains of BSE, different types of cattle *etc*.

See comment 2.8. Dr. Cox does not present any evidence that these possibilities are likely or even plausible. The questions of possible BSE strains or differential susceptibility of cattle breeds to BSE are discussed in the Harvard BSE report (Cohen 2003).

Appendix 3: Cohen, J. and G.M. Gray, Harvard Center for Risk Analysis, Response to Comments Submitted in Response to USDA's Proposed Rule on Importing Beef and Beef Products from Canada. Memorandum submitted to USDA on June 18, 2004.

Appendix A Detailed Simulation Results

Table A-1 details the summary statistic estimates and confidence intervals for the R_0 parameter based on the simulations described in Section 1 of this memo. The 95% confidence intervals account for the uncertainty introduced by the use of a finite number of simulation trials (N = 5,000) to characterize the distribution of R_0. The The 95% confidence intervals for the quantiles were computed using SAS PROC Univariate, option CIPCTLDF (SAS version 8.2 for Windows, SAS Institute, Cary, North Carolina). This routine uses a distribution-free method to estimate the confidence intervals for quantiles and is based on the algorithm detailed in Section 5.2 of Hahn and Meeker (1991). The confidence interval for the mean was computed using SAS PROC Univariate, option CIBASIC.

Table A-1
Summary Statistics for R_0

Assumed Misfeed Rate	Summary Statistic	Central Estimate	95% Lower Confidence Limit	95% Upper Confidence Limit
0%	Mean	0.08	0.08	0.09
	5%	0.01	0.01	0.01
	25%	0.02	0.02	0.02
	50%	0.03	0.03	0.03
	75%	0.06	0.05	0.06
	95%	0.39	0.39	0.40
2.5%	Mean	0.22	0.21	0.23
	5%	0.01	0.01	0.01
	25%	0.04	0.03	0.04
	50%	0.09	0.08	0.10
	75%	0.40	0.39	0.40
	95%	0.64	0.62	0.65
5%	Mean	0.35	0.34	0.36
	5%	0.02	0.02	0.02
	25%	0.07	0.07	0.08
	50%	0.37	0.37	0.38
	75%	0.58	0.57	0.59
	95%	0.81	0.80	0.82

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Assumed Misfeed Rate	Summary Statistic	Central Estimate	95% Lower Confidence Limit	95% Upper Confidence Limit
7.5%	Mean	0.49	0.48	0.50
	5%	0.04	0.03	0.04
	25%	0.17	0.15	0.19
	50%	0.53	0.50	0.55
	75%	0.76	0.75	0.77
	95%	0.95	0.94	0.96
10%	Mean	0.63	0.62	0.64
	5%	0.06	0.06	0.06
	25%	0.40	0.38	0.41
	50%	0.70	0.68	0.72
	75%	0.91	0.90	0.92
	95%	1.06	1.05	1.07
12.5%	Mean	0.78	0.77	0.79
	5%	0.09	0.09	0.10
	25%	0.59	0.57	0.61
	50%	0.88	0.87	0.90
	75%	1.03	1.02	1.03
	95%	1.15	1.14	1.15
15%	Mean	0.91	0.91	0.92
	5%	0.16	0.15	0.19
	25%	0.80	0.77	0.82
	50%	1.03	1.02	1.03
	75%	1.13	1.13	1.14
	95%	1.23	1.22	1.23

Appendix 3: Cohen, J. and G.M. Gray, Harvard Center for Risk Analysis, Response to Comments Submitted in Response to USDA's Proposed Rule on Importing Beef and Beef Products from Canada. Memorandum submitted to USDA on June 18, 2004.

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